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CALCIUM DEPOSITS IN THE VICINITY OF THE SHOULDER AND OF OTHER JOINTS*

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THE OCCURRENCE of localized deposits of calcium in the supraspinatus tendon in the floor of the subdeltoid bursa is a well-known clinical condition and during the past 30 years many papers have been published on the subject. This literature is reviewed by Codman[1] and Wilson.[2]

It is not so well known, however, that similar deposits of calcium may occur in the other tendons of the shoulder girdle and in the vicinity of other joints. The only paper that I have found in the American medical literature describing calcium deposits about various joints other than the shoulder is that by Hitchcock,[3] in which nine cases are reported: Knee—two (one in the capsule above the head of the fibula and one in the quadriceps tendon above the patella); hand—three (two adjacent to the metacarpophalangeal joint of the fifth finger); wrist—one (distal to the head of the ulna); hip—one (mesial to the trochanter and superior to the joint capsule); elbow—one (in the joint capsule adjacent to the lateral epicondyle); and near the ankle—one (lateral to the external malleolus).

On the other hand, three papers describe localized deposits of calcium in the vicinity of certain specific joints. Milch and Green[4] report five cases of calcification about the flexor carpi ulnaris tendon and regard this condition as a distinct clinical entity. Mauritz[5] reported one case of acute intermetacarpophalangeal calcification with redness and swelling of the hand.

Goldenbert and Leventhal[6] reported five cases of calcified deposits above the trochanter, apparently in the tendon of the gluteus medius muscle, and stated that similar deposits were seen in the roentgenograms of 30 of the hips of 550 patients which they examined. One of these cases was operated upon, and the tissues above the trochanter were found to contain a plaque of bone two inches long by one and one-fourth inches wide. Nilsonne[7] also reported a case of calcification in the gluteus medius tendon in which some true bone formation was present in the tendon in association with the calcium deposits. Sandstrum and Wahlgren[8] reported 12 cases of calcareous peritendinitis in which the shoulder was involved eight times, the hip twice, the knee once and

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the heel once. As will be noted below, we believe that these calcium deposits in various locations are similar to one another and can be grouped together rather than regarded as separate clinical entities.

INCIDENCE

The occurrence of calcium in the region of the shoulder is a relatively frequent condition and one which is often associated with stiff and painful shoulders, periarthritis and tendinitis of the shoulder, or subdeltoid or subacromial bursitis. McLaughlin[9] states that almost 2,000 lesions which are commonly diagnosed and treated as "calcified subdeltoid bursitis" were studied by the fracture service of the Presbyterian Hospital over a period of 15 years. Dickson and Crosby[10] found that 73, or 36.5 per cent, of 200 cases of periarthritis of the shoulder showed deposits of calcium which were visible in the roentgenograms. In a study of 6,061 unselected adults who were subjected to fluoroscopic examinations, Bosworth[11] found calcium deposits in one or both shoulders in 165, or 2.7 per cent. Of 138 such individuals who were company employees and on whom accurate records were available, the deposits were bilateral in 46.4 per cent; thus, calcium was present in 202 shoulders. In these patients, symptoms referrable to the shoulder were present at one time or another in 70 shoulders, or 34.6 per cent, while the remainder were quiescent and caused no symptoms during the three-year period of observation.

On the other hand, calcium deposits in the vicinity of joints other than the shoulder are relatively rare, or at least not many such cases have been reported in the literature. During the past 10 years I have encountered 20 patients with deposits of calcium in locations other than in the musculotendinous cuff of the shoulder. These were distributed as follows: coracoid process, 1; elbow, 4; wrist, 3; hand, 4; (all adjacent to a metacarpophalangeal joint); hip, 4; knee, 2; and foot, 2 (adjacent to the second metatarsophalangeal joint and heel). These were all in different patients.

ETIOLOGY

Wells[12] states that calcification seldom occurs in normal tissue except in the formation of bone but that any area of dead tissue that is not infected and that is so large or so situated that it cannot be absorbed, will probably become infiltrated with lime salts. Exceptions to this rule are the metastatic calcification of Virchow, which occurs in individuals in whom the blood is oversaturated because of calcium absorption from the skeleton, and calcificans universalis. But in normal individuals it appears that local degeneration of the tissue precedes the deposition of the lime salts.

Determination of the calcium, phosphorus and alkaline-phosphatase content of the blood in several of our patients with local deposits of calcium has failed to reveal anything abnormal, and this has also been the experience of other observers. Consequently we must assume that in these patients with deposits of calcium about joints degeneration of the involved tendon or of the ligament or capsule of the joint preceded the deposition of calcium and that the primary cause of the trouble is the cause of the degeneration.

However, the fact that the deposits are so frequently bilateral in the shoulder (46.4 per cent in Bosworth's larger series) suggests that there may be some constitutional predisposition to the deposition of calcium in the vicinity of joints which is so slight a variation from the normal that we have not yet succeeded in detecting it. Another possibility is that in certain individuals the musculotendinous cuff is predisposed to degeneration, either because of some anomaly in the structure of the shoulder which exposes it to injury or because of inherent weakness of the tendon. Dickson and Crosby believe that deposition of calcium is determined by some underlying alteration in the physical state, which is influenced by foci of infection and by endocrine irregularities.

It has been noted by Codman and others that the onset of symptoms may follow an injury or that the symptoms may begin spontaneously without any known cause. Since we know that silent or asymptomatic calcium deposits are not uncommon, it is probable that the single injury which is alleged to have caused the deposit may have aggravated or produced symptoms in a silent deposit. It is possible that the trauma may injure the tissue surrounding a silent deposit and cause the calcium to spread to tissue where it can cause symptoms. On the other hand, it also seems possible that an injury may have caused the degeneration which laid the foundation for the calcium deposit. Bishop[14] believes that minor traumas may cause rupture of a few fibers of a tendon (supraspinatus) with few or no symptoms and that these may heal but that frequent repetition of the injury may lead to hyaline degeneration and the depositing of calcium in these areas. Bosworth's figures indicate that occupations which involve excessive use of certain muscles, as, for instance, the supraspinatus in typists, may predispose to the formation of calcium deposits in the tendons of their muscles, and that these may appear within two months or less.

The calcium salts are withdrawn from the blood, where they are held by the proteins in an unstable state of suspension or solution. It is believed that the increased alkalinity or decreased carbon dioxide which is present in degenerating or necrotic tissues causes the calcium carbonates and phosphates in the fluids which are seeping through these tissues to be precipitated. Klotz[13] believed that the deposition of the calcium is preceded or accompanied by the formation of soaps in the degenerating tissue and that these withdraw the calcium from the body fluids and that the fatty acids are then replaced by carbonic and phosphoric acids to form more stable carbonates and phosphates of calcium. Wells does not accept the view that the formation of calcium soaps constitutes an essential step in pathologic calcification and states that it is probable that there are no essential differences between this and normal ossification.

PATHOLOGY

In pathologic calcification the calcium phosphates and carbonates are in the same proportion as in the bone. The substance first appears as minute amorphous granules which are scattered irregularly through the degenerating tissue or fibrin matrix. These coalesce to form spherules or larger masses

FIG. 1

A B

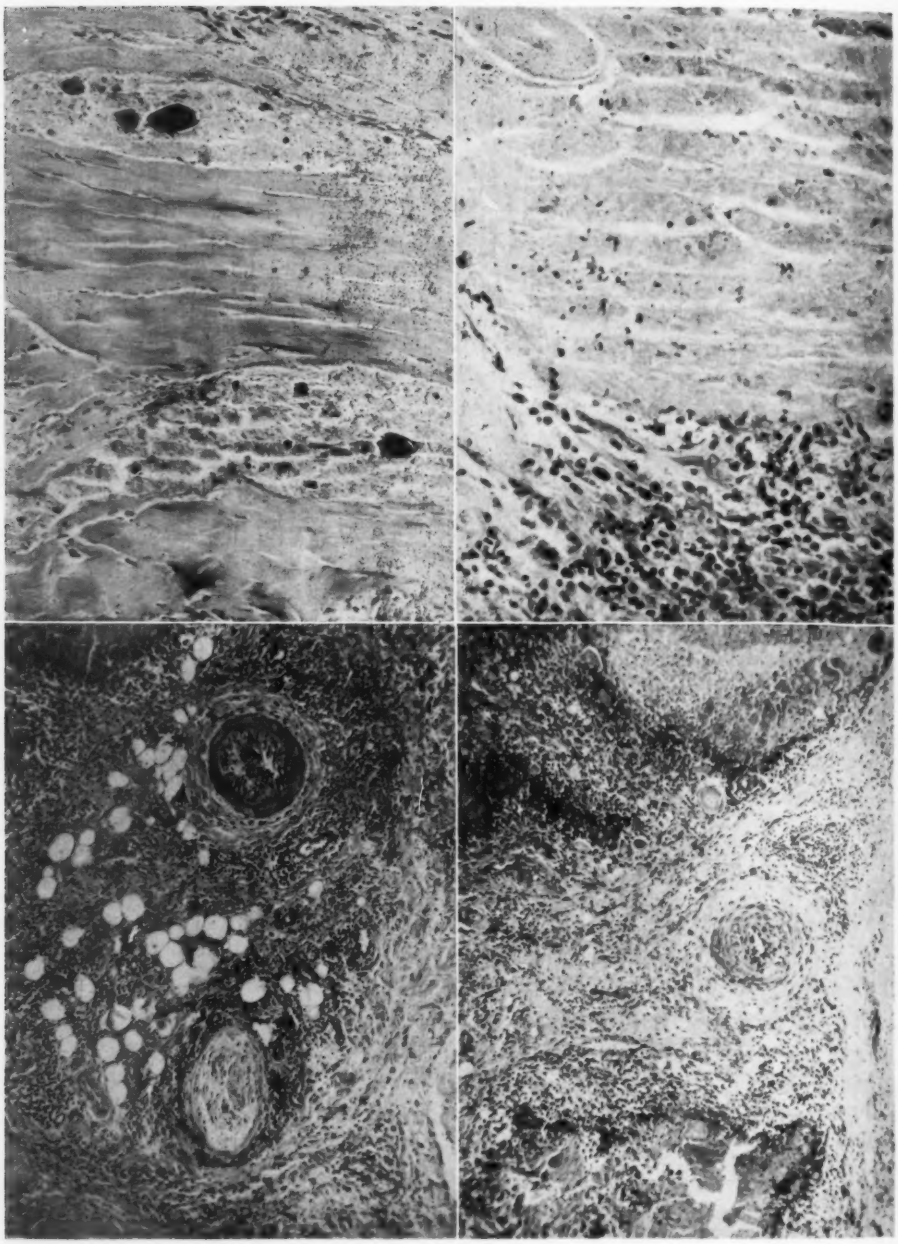


FIG. 2

A B

FIG. 1.—(A) Small calcium deposits in fibrous tissue adjacent to the elbow in which the form of the fibers appears to be preserved by the degenerated material. x 110. (B) Larger mass of calcium deposit from the same lesion with cellular infiltration of the degenerating tendon. x 225.

FIG. 2.—(A) Subacute inflammation with round-cell infiltration in areolar tissue adjacent to the elbow. The artery above and the nerve below and a bit of a calcium deposit are seen in the upper left-hand corner. x 75. (B) Artery and round-cell-infiltrated fibrous tissue lying between two large calcium deposits from the same specimen. x 70.

FIG. 3

A B

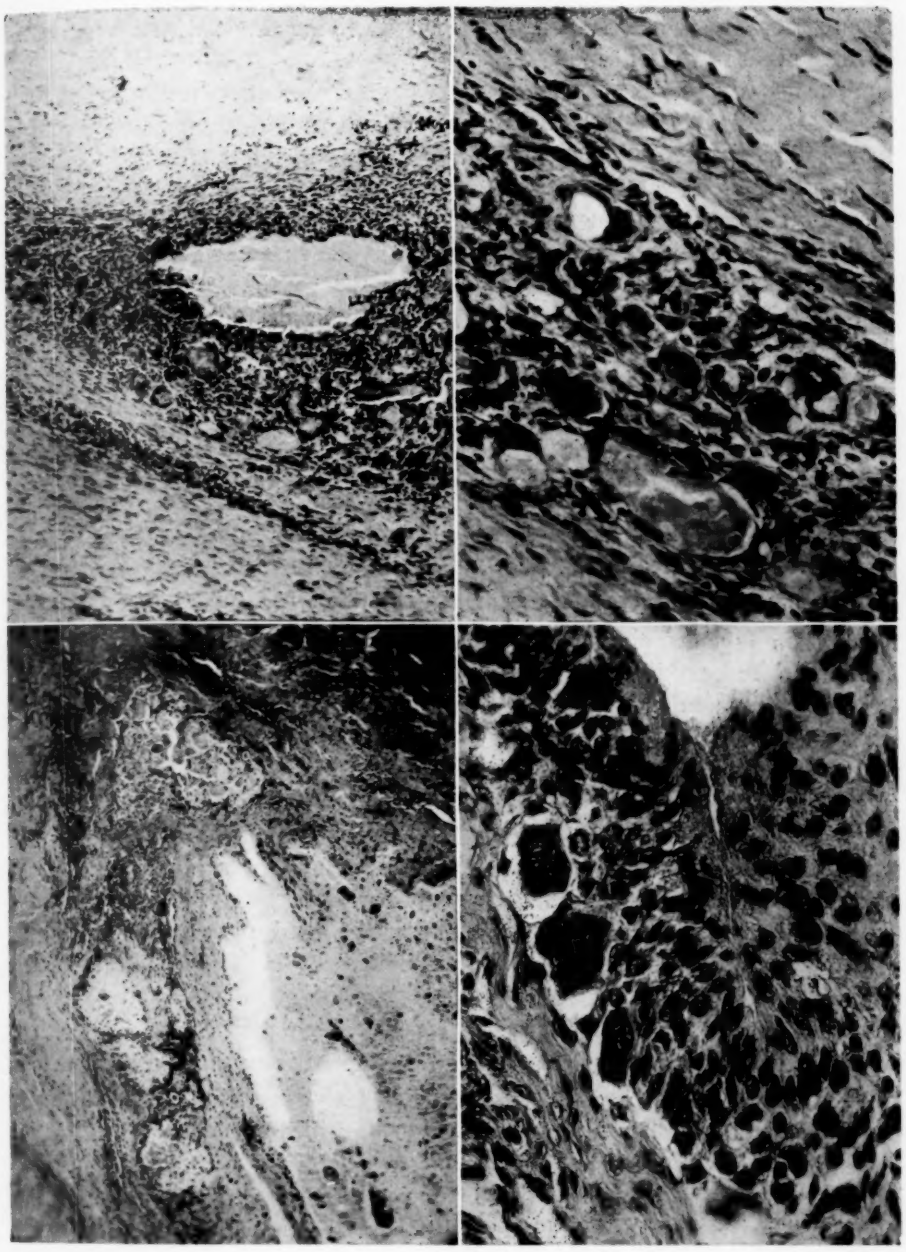


FIG. 4

A B

FIG. 3.—(A) Calcium deposit in the supraspinatus tendon with giant cells and round-cell infiltration. x 70. (B) Higher-power photomicrograph of a smaller similar deposit in an apparently normal tendon from the same specimen. x 225.

FIG. 4.—(A) Large and smaller cystlike areas containing calcium and degenerated tissue debris in a chronic lesion of the supraspinatus tendon. x 45. (B) High-power photomicrograph of a portion of the wall of a similar lesion adjacent to the elbow. Note the small giant cells and what appear to be modified fibroblasts lining the cavity. x 300.

which are scattered through the tissue or mixed with the organic ground substance which is presumably the disintegrating remains of the degenerated tissue, but there is no diffuse infiltration of a living tissue with calcium salts such as occurs in the formation of bone.

The gross appearance of the deposit when exposed at operation varies with the location and duration of the deposit as well as with the condition of the surrounding tissue. We have operated upon approximately 50 calcific deposits in the musculotendinous cuff of the shoulder and on nine of the 17 cases which are reported here as having occurred in the vicinity of other joints.

In our experience, the calcium deposits in the shoulder vary considerably in size, number and location as well as in the consistency of the calcified material. Bosworth found that 51.5 per cent of the involved shoulders had deposits in the supraspinatus portion of the cuff, 44.5 per cent in the infraspinatus, 23.3 per cent in the teres minor. Only five shoulders showed calcium in the subscapularis and 25 showed calcium in the subacromial bursa. Multiple deposits occurred in 20.3 per cent of the involved shoulders. We have not attempted to record the locations of the deposits in our shoulder cases.

A fairly typical operative finding in an acute case is for the floor of the subdeltoid bursa to present a domelike swelling about two centimeters in diameter. The apex or center of this furunclelike swelling is white and this is surrounded by a purplish or red inflammatory zone, which shades off into the slightly inflamed floor of the bursa. When the apex of this swelling is incised, white or yellowish-white material of the consistency of tooth paste exudes on the floor of the bursa. When the remainder of the calcific material is removed with a curette, a cavity is left in the tendon which has a ragged avascular surface; this may be so deep that it appears to extend down through the tendon into the underlying bone.

In some hyperacute cases of short duration, the calcific material is thin or milklike in consistency and may be under such pressure that when the surface of the tendon is incised, the contents of the deposit may spurt into the air. In others the deposit may have ruptured into the bursa and the bursa may be found to be distended with a thin, milklike fluid. In chronic cases, the calcium deposit may be inspissated, and upon incising the tendon, the surgeon encounters one or more dry, chalky deposits which can be removed with a curette. There are all gradations between the types of deposit described above.

It is probable that the deposits are nearly always multiple and that the surgeon never sees many of the small deposits which are buried deep in the tendinous floor of the bursa. We have encountered many such minute deposits in microscopic sections of apparently normal tendon from the floor of the bursa. Likewise, the moderately large deposits (0.5 cm. or more in diameter) may exist in the same musculotendinous cuff.

In deposits in areas other than in the musculotendinous cuff of the shoulder, it has been my impression that the calcium was not under tension in the tendon or ligaments but was in a thin-walled cavity or free in the adjacent areolar tissue.

The microscopic picture varies with the state of inflammation in the tissues adjacent to the calcium deposits. Since most of the sections which I have studied were taken from acutely inflamed lesions, I have not been impressed with appearances of degeneration or even with relative avascularity in these tissues. Frequently in tendons the small calcium deposits may be present as spindlelike collections of granular material surrounded by apparently normal tendon fibers. In adjacent areas the fibers may be fragmented and curled or hyalinized or may appear normal.

More frequently than not, the tissue was more vascular and more cellular than normal. In most instances in which the operation was performed for moderately acute pain and disability, the tissue adjacent to the calcium deposit was infiltrated with small and medium-sized round cells (monocytes or epithelioid cells). Some of these cells were present in the necrotic tissue debris which was mixed with the calcium deposits. Small foreign-body giant cells were also present here. In the lesions of longer duration, the giant cells were larger and more numerous. The absence of blood pigment in the tissues and in the macrophages suggests that the lesion had not been the site of a previous hemorrhage and thus was probably not traumatic in origin. In harmony with the accumulation of round cells in the area, there was proliferation of the fibroblasts and an increase in the vascularity in the tissue adjacent to the deposits.

In the hyperacute lesions with severe pain and disability, large numbers of polymorphonuclear leukocytes were present in the calcium deposits and in the surrounding tissues and many of these cells were disintegrating. Likewise, in some of the acutely inflamed deposits near joints other than the shoulder, the areolar tissue contained fibrin and this was infiltrated with leukocytes and round cells.

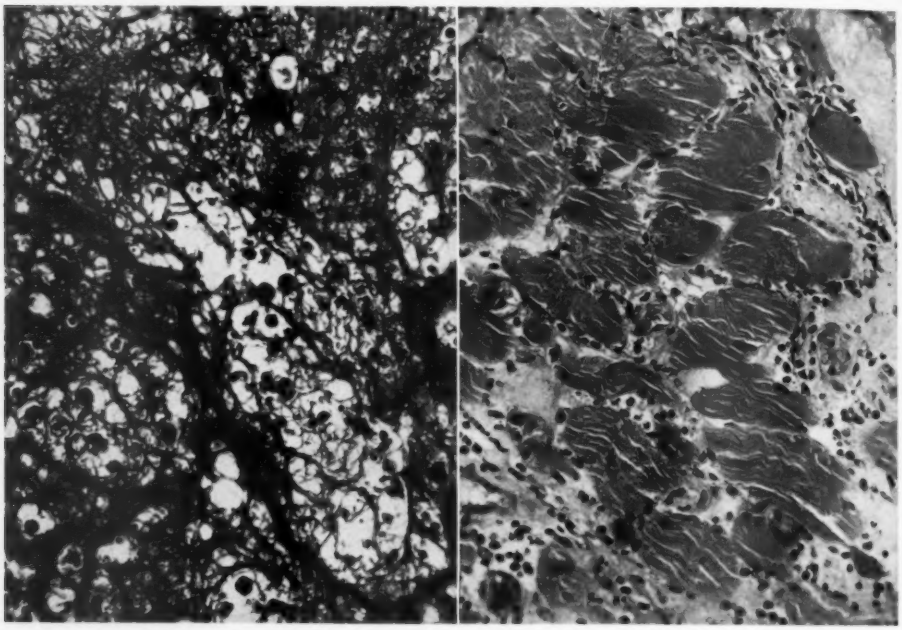
In some of the more chronic cases in the shoulder rather large, cystlike cavities which contained debris and calcium were surrounded by a definite wall of chronic inflammatory tissue. Cultures from these deposits have been sterile and there is no indication that infection plays any part in the process. The inflammation is apparently due to chemical irritation and foreign-body reaction.

In locations other than the musculotendinous cuff of the shoulder, the calcium deposits have been found in the areolar tissue superficial to a tendon or ligament near its attachment to bone or in the musculotendinous origin of muscles near the bone. The deposits may have begun in the dense connective tissue and extended outward but were not found there at operation. Consequently, the dense connective tissue of the tendon is usually absent from the microscopic sections and areolar tissue may be found in the vicinity of the calcium deposits. No other difference was found between the microscopic picture of the lesions in the shoulder and those in the vicinity of other joints.

SYMPTOMS AND CLINICAL COURSE

It is probable that these calcific deposits begin as microscopic precipitates of calcium salts which gradually increase in size until they encroach upon the

surrounding tissues and cause an inflammatory reaction there. Such a calcium deposit may be present in the tissues for months or even years and cause no symptoms and then suddenly, after an injury or without any known precipitating cause, may become the central point of an area of acute inflammation, with severe pain and disability. The reason for this is not known. The inflammation is the cause of the symptoms. Apparently the process is a reversible phenomenon and the calcium may be resorbed either spontaneously or as a result of the inflammatory reaction. Whether these primary deposits are in the cells, between the connective-tissue fibers or in the fibers has not been determined satisfactorily. As they increase in size, the calcium is mixed with debris of degenerating connective-tissue fibers and cells.



A B

FIG. 5.—(A) Coagulated fibrin infiltrated with degenerating round cells and leukocytes from a hyperacute lesion mesial to the coracoid. (B) Hyalinization and fragmentation of fibers of the teres minor muscle, with infiltration by leucocytes and round cells in a hyperacute lesion.

It is evident that most, if not all, of these deposits are silent or asymptomatic in the beginning and it is probable that the majority of them slowly attain a moderate size, persist for an indefinite period and then disappear without causing symptoms. In Bosworth's series only 70, or 34.6 per cent, of the involved shoulders had been the seat of pain or discomfort either prior to or during the three-year period of observation. He also noted that the larger deposits (1.5 cm. or larger in diameter) tended to cause symptoms and that the size of the deposit tended to be in accord with the symptoms, yet one-third of the large deposits in his series gave rise to no complaints during the period of observation. Howorth,[15] however, states that large deposits may be almost

symptomless while small deposits may be associated with considerable pain. He further states that deposits may change in size and density within a few days.

The symptoms are those of local inflammation in the involved area; that is, pain and disability, and these vary greatly in degree and are sometimes classified as hyperacute, acute, subacute and chronic, depending upon the intensity and the duration of the symptoms. In a hyperacute case, the onset may be abrupt with severe, throbbing pain in the shoulder which prevents the patient from sleeping or even from remaining in bed. The pain may remain sharply localized or may spread up over the side of the neck and behind the shoulder and down the arm to the insertion of the deltoid muscle and even to the fingers. It is aggravated by the slightest movement of the extremity or by pressure over the front of the shoulder or by local heat. Such patients may require opiates for relief of the pain.

In the average acute case, the pain begins gradually, sometimes following a direct blow or unusual strain or prolonged use of the shoulder, but usually without a preceding injury, and increases slowly over a period of several days until the patient is troubled by an almost constant dull ache in the shoulder which is aggravated by movement or pressure or the application of local heat. Unless the condition subsides spontaneously or is relieved by treatment, the pain tends to spread up over the side of the neck, down over the scapula, and it centers especially at the insertion of the deltoid and may extend down to the fingers. As in many other conditions, the pain is worse at night.

The patient tends to hold the arm fixed to his side, with the forearm supported across the chest. Bishop has noted that this condition resembles that described as the scalenus syndrome and suggests that the referred pains are due to reflex spasm of the scalenus anticus muscle. With the passage of time, the movements of the shoulder, especially internal or external rotation and abduction, become progressively limited and the muscles of the shoulder become atrophied. At first, the limitation is due to muscle spasm, but later structural changes occur in the capsule and periarticular tissues and fix the humerus to the scapula, and the atrophy involves not only the muscles but also the bones and especially the greater tuberosity of the humerus. This severe, painful, disabling condition may continue for months or may subside spontaneously at any time.

Many patients never have severe pain or disability but complain of occasional painful catches in the shoulder with certain movements, especially abduction or rotation, and of inability to sleep on the affected side. These subacute symptoms may persist or recur at intervals over periods of months or years.

The findings on physical examination vary with the symptoms. In a patient with hyperacute symptoms the arm is held close to the side and the forearm may be supported across the chest. There may be slight swelling of the front of the shoulder, and the area over the anterior surface of the greater tuberosity of the humerus is quite tender and an exquisitely tender point can be localized. The patient objects to attempts to move the arm in any direction, but usually a moderate amount of forward flexion can be carried out passively without

causing much pain. There may be a moderate increase in temperature and the white blood-cell count may be moderately elevated.

In the average acute case of short duration, the appearance of the shoulder is normal. Palpation reveals a small area of acute, sharply localized tenderness over the anterior surface of the greater tuberosity of the humerus just below the anterior margin of the acromion. This point of tenderness may be located mesially over the tendon of the long head of the biceps or laterally over the infraspinatus tendon. The tenderness is most marked directly over the calcium deposit and if this is in the tendon of the teres minor, the point of maximum tenderness is more distal and more lateral on the shoulder. The arm is held at the side and the patient does not object to a moderate amount of manipulation, but the range of movement in rotation or abduction is moderately limited and causes pain, while movement in flexion or extension is fairly free and painless.

A B

FIG. 6.—(A) Knee joint with a calcium deposit adjacent to the intercondyle of the femur. This produced severe pain and disability and was operated upon early, with complete relief. (B) Calcium deposit adjacent to the intercondyle of the femur. This failed to yield to conservative treatment over a period of three and one-half months and was operated upon, with complete relief of symptoms.

In cases with severe symptoms and of longer duration, the pain and tenderness involve a wider area, and there may be tenderness on deep pressure over the side of the neck (scalenus anticus muscle and the cords of the brachial plexus), over the superior angle of the scapula and over the insertion of the deltoid. The atrophy of the muscles of the shoulder is evident on inspection and palpation and if the scapula is fixed and the arm manipulated it will be found that there is very little scapulohumeral movement and that movement of the extremity is accomplished by movements of the scapula on the thorax.

The subacute case may present nothing on physical examination except an area of moderate tenderness over the front of the tuberosity and a painful catch with certain movements of the arm. Usually the catch is felt when the arm is lowered actively to the side from a position of abduction and external

rotation. It seems to be produced by the painful area sliding under the margin of the coraco-acromial ligament.

The calcific deposits in the vicinity of other joints produce local pain and disability, which vary in intensity from time to time and in different cases just as occurs in the shoulder. For instance, the small calcium deposit over the internal lateral ligament of the knee shown in Figure 6(a) had caused symptoms for only three days, but the pain was so severe that the patient was confined to bed and maintained the knee in a position of acute flexion, and he complained bitterly when an attempt was made to straighten the extremity or when pressure was made over the painful area. He was operated upon one Sunday afternoon as an emergency case in order to relieve the intense pain. The other quite similar deposit in this area, shown in Figure 6(b), occurred in a large, active woman. It interfered very little with the patient's activities and was observed and treated conservatively over a period of more than three months and finally was operated upon because of persistent annoying pain and tenderness.

Of the other deposits not in the musculotendinous cuff which I have operated upon, the two at the shoulder (one in the teres-minor muscle posterior to the humerus and one mesial to the tip of the coracoid) were operated upon to relieve severe acute pain of short duration. The others (three at the elbow, one at the wrist and one in the hand) were operated upon on account of persistent mild pain, tenderness and disability which did not subside under conservative treatment.

One of the cases of a deposit adjacent to the flexor carpi ulnaris tendon reported by Milch and Green was of the hyperacute type, with swelling of the wrist and red streaks extending up the arm resembling lymphangitis. Likewise, the case at the metacarpophalangeal joint reported by Mauritz presented considerable swelling of the hand. Such very acute cases may exhibit a moderate elevation of temperature and of the leucocyte count. In the usual case, however, there is no swelling or redness, the pain is moderate in degree and is produced by local pressure, or movements which cause tension or increased pressure in the involved area, and there are no general symptoms.

THE ROENTGEN FINDINGS

The presence of a localized deposit of calcium in the tissues may be suspected, but the diagnosis is not made unless the material can be visualized in the roentgenogram. From what has been written above, it is evident that the deposits vary considerably in size and density. Many small ones will not cast a shadow and cannot be seen with the fluoroscope or in the roentgenogram. Consequently, these cannot be diagnosed clinically. Larger deposits may be obscured by overlying bone. This is especially true of the musculotendinous cuff of the shoulder, where the calcium may be spread out in a thin layer and may not cast a shadow dense enough to be seen through the bone or even through thick soft tissue, unless it is seen in profile.

Bosworth advises that the shoulder be examined under a fluoroscope while the arm is carried through the full range of movement. Then if calcium

deposits become visible, spot films are made in order to visualize them more clearly and record their position. However, most calcium deposits in the musculotendinous cuff of the shoulder will be seen in a film taken with the arm at the side and in a position of external rotation. We routinely have a second anteroposterior exposure made with the arm rotated inward, and occasionally a third inferior-superior or vertical view with the film on top of the shoulder.

In joints other than the shoulder the calcium can be shown roentgenographically with less difficulty and is usually visible in the routine films taken in two planes. It tends to vary in density with the duration of the symptoms; the image being more dense in instances in which the symptoms have been present for a longer time. The margins of the deposit tend to be poorly defined on the roentgenogram and the density may be irregular. It can usually be differentiated from bone by the fact that it shows no evidence of internal structure.

FIG. 7.—Wrist joint with faintly visible calcium deposit distal to the styloid of the ulna. This cleared up promptly after deep roentgenotherapy.

TREATMENT

The treatment of calcium deposits varies with the severity of the symptoms and with the tolerance of the patient for the symptoms. If the deposit is discovered accidentally and is causing no symptoms, no treatment is indicated. If the deposit is causing sufficient pain and disability to lead the patient to consult a physician for relief, then treatment is indicated and this may either be conservative or radical measures may be instituted.

Conservative treatment is largely palliative. Its success is based on the fact that in practically all these cases the pain will subside if the patient can wait long enough, and in most instances function will be restored to the part. It is probable that the inflammatory reaction which causes the symptoms also results in an increased vascularity in the area and that this tends to promote resorption of the deposit. For this reason, the hyperacute symptoms rarely last very long. However, though these symptoms may lessen to a point where they are tolerable, they may still be the cause of much pain and disability and may result in chronic stiff and painful shoulders persisting for many months or even years. It is questionable whether or not any form of conservative treatment actually influences the course of the disease or causes resorption of the deposit.

The conservative measures in use are: local heat, local cold, immobilization, exercises, sedatives and deep roentgen therapy.

Local heat may be applied as moist heat from hot compresses, or dry heat

from an electric pad, hot-water bag, infrared lamp or diathermy. If the symptoms are severe, heat may aggravate the pain. In many cases, however, heat has a soothing effect and it may enable the patient to sleep. Some surgeons believe that diathermy may actually promote the resorption of the deposit. I have not seen this occur and believe that long-continued diathermy may be harmful.

Local applications of cold, as cold compresses or an ice bag, may give considerable relief to patients with severe pain.

Immobilization of the part in a sling or bandage or by strapping or even by a plaster of Paris splint or cast may afford some relief but should be avoided with lesions in the shoulder as it encourages stiffness of this joint which may be difficult to overcome.

Exercises are useful in restoring function to the part after the acute symptoms have subsided. They are especially helpful in chronic lesions of the shoulder. Passive stretching by continued traction is used in some cases with frozen shoulders. As much sedation as is necessary is given while the traction is acting.

Sedatives are used as indicated for pain. Salicylates and codeine are useful, either alone or in combination, and we give the patients large doses of vitamin B.

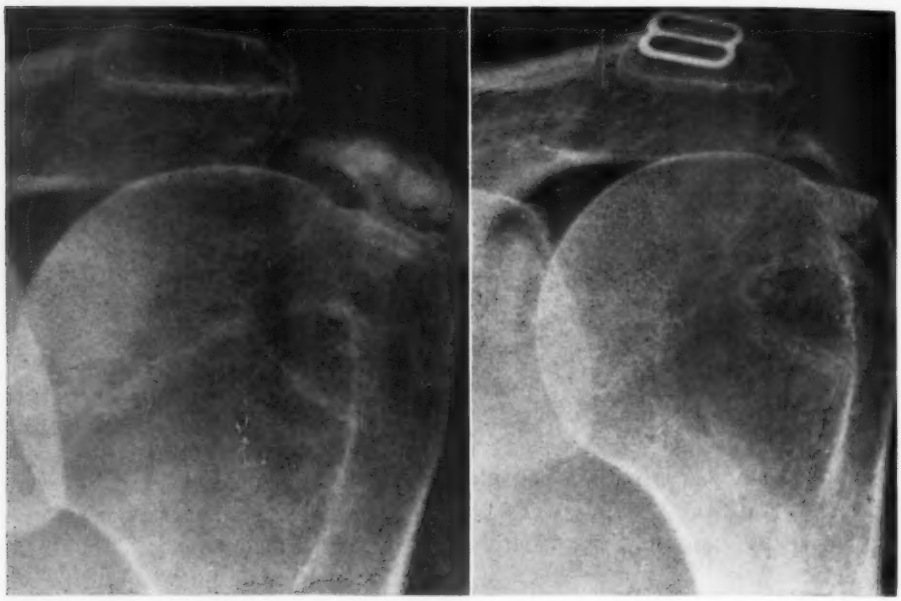
Deep roentgenotherapy has been used quite extensively during recent years and there are reports in the literature in which it is recommended as an almost infallible cure for calcium deposits in the musculotendinous cuff of the shoulder. I have advised it for a considerable number of patients during recent years but am still not in a position to make a statement concerning its efficiency. In some mild or moderately severe cases deep roentgen treatment has seemed to afford some relief while in others it has had no apparent effect. In hyperacute cases with severe pain, it has not appeared to do any good. The same is true of chronic cases, and especially when there are severe capsular adhesions or contractures. In the latter the roentgenologist should restrain his enthusiasm or burns may be the result.

The more radical methods of treatment are manipulation under general anesthesia, needling with or without irrigation and operative exposure and removal of the deposit.

Manipulation under general anesthesia is used in breaking up the adhesions and restoring movement to shoulders with marked limitation of motion. After the patient is relaxed by the anesthetic, the arm is abducted fully and then rotated externally and internally while the scapula is fixed to the chest by an assistant. It is desirable that the arm be carried through the complete range of movement. If a calcium deposit is present, the manipulation should be combined with open operation for removal of the deposit. The manipulation is not without danger, as the anterior and inferior portions of the capsule are usually torn if the limitation of motion is marked, and the shoulder may be dislocated or the humerus may be fractured. After the manipulation, the pain may become aggravated and the adhesions may recur unless this is prevented by stretching and exercise. During the first few days, the patient is kept in bed

with the arm in abduction and external rotation. (The wrist is tied to the head of the bed.)

Needling of the deposit is a procedure which was quite popular a few years ago and is still used in some clinics. It is most useful in an acute case with a single relatively large deposit. Under local or general anesthesia a relatively large (18- or 16-gauge) needle is introduced into the deposit and as much as possible of the calcium-containing material is aspirated. Then multiple punctures are made in the area in order to produce inflammation and stimulate



A B

FIG. 8.—(A) Unusually large calcium deposit in the musculotendinous cuff of the shoulder. The duration of symptoms was about two and one-half years, with several acute episodes. (B) A view of the same shoulder, as shown in Figure 8A immediately after operation, shows that a considerable amount of calcium was missed and left in the shoulder, but the patient was relieved of her symptoms by the operation. It is believed that the remaining calcium will disappear gradually.

absorption of the remainder of the calcium. In the shoulder this may be combined with irrigation of the subdeltoid bursa either with or without a second needle in the bursa. In my hands, needling is done under local anesthesia and is used for those patients when operative removal of the deposit is indicated but who do not wish to be operated upon. It is apt to be followed by a few days of severe pain and is not as reliable a form of treatment as is the operative removal of the deposit.

Operative removal of the deposit is the surest method of affording the patient prompt and permanent relief. It is especially indicated in patients with severe pain and multiple deposits or with one small deposit which is difficult to enter with a needle or in patients who have failed to obtain relief after a needling procedure.

OPERATIVE TECHNIC

If the deposit is in the shoulder, the operation may be performed under local or general anesthesia, with the patient supine on an ordinary operating table or in the sitting position, preferably in a dental chair with a support for the head. Abbott[16] recommends local anesthesia and the sitting position because the arm can be moved actively by the patient and the areas of tenderness can be more accurately localized after the bursa is opened. This is especially true of those deposits which lie deep in the tendon and cannot be seen on inspection.

The point of maximum tenderness should be noted before the operation and the incision should be made directly over this point. The incision begins over the margin of the acromion and extends downward for about two inches over the point of maximum tenderness. The deltoid fibers are split to expose the wall of the bursa and this is incised, or a window about one inch square may be removed to expose the musculotendinous cuff which forms the floor of the bursa. The calcium deposit which is causing the trouble is usually visible as an elevated inflamed area with a white or yellowish center. This is incised in line with the fibers of the tendon, the contents are allowed to escape and a specimen of the wall of the cavity is removed.

The cavity containing the calcium is then scraped lightly with a curette, but no attempt is made to remove all the calcium, as this infiltrates the surrounding tendon and its removal would entail extensive damage to the tendon and do more harm than good. It is probable that merely incising and draining the deposit is all that is necessary for a cure, as this will lead to resorption of the remainder of the calcium.

The shoulder is then rotated inward and outward to expose more of the floor of the bursa, and any other suspicious areas in the tendon are incised in a similar manner; if calcium deposits are found, the larger ones are curetted lightly while the smaller ones are simply drained by the incisions. These multiple, short incisions parallel with the tendon fibers are not sutured and seem to heal without disability. They may reveal deposits which would not have been seen otherwise. Also it is evident that in many shoulders there are deposits which are not drained by the operation, as the surgeon must avoid doing any more harm than necessary.

In some cases, no deposit or elevation of the floor of the bursa is visible and in such instances one or more parallel incisions are made through the tendon until the deposit which is being sought is entered and its contents are then evacuated. The surgeon should endeavor to evacuate all large deposits and especially those that are causing the symptoms.

After the larger calcium deposits have been incised and evacuated, the surgeon manipulates the shoulder into full abduction and internal and external rotation in order to break up adhesions which may have formed. This is especially important in cases of long duration, with limitation of movement due to structural changes, and may require a small amount of pentothal or

other general anesthetic if the operation is being performed under local anesthesia.

The wound is then closed in layers and covered with a small gauze dressing.

POSTOPERATIVE TREATMENT

In the acute cases, no immobilization is necessary and the patients may leave the hospital a day or two after the operation and return for removal of the sutures on the sixth postoperative day. They are encouraged to use and exercise the arm, and usually the normal range of movement is obtained within a few weeks.

In the chronic cases with adhesions and which have been manipulated, it is advisable to immobilize the arm in abduction and external rotation for a few days after the operation. This can be accomplished by tying the wrist to the head of the bed. The arm is then lowered and pendulum and abduction exercises are prescribed; these may be combined with some passive stretching. The treatment may be continued until a satisfactory result is obtained, which may require several weeks.

Deposits about other joints are treated in the same way as those in the shoulder; that is, conservatively or operatively, depending upon the severity of the symptoms and the wishes of the patient and surgeon. At operation, the deposit is approached by the most direct route, it is incised and curetted lightly and the wound is then closed. They require no special postoperative treatment. The nine patients on whom I have operated in this manner have been relieved of their pain promptly and the condition has not recurred.

PROGNOSIS

As was stated above, the deposition of calcium in the tissues is a reversible process and the calcium may be resorbed spontaneously without causing symptoms or after causing variable amount of pain and disability. It is believed that the inflammation which gives rise to the symptoms causes an increased blood supply in the area and that this hastens the resorption of the calcium. Consequently the very acute symptoms rarely last very long.

In some cases the symptoms subside completely and in others a variable amount of pain and disability remains, which may persist for many months.

In severe cases, needling or operative removal of the deposit is often the treatment of choice; the latter usually results in a fairly prompt relief of pain and restoration of function to the extremity. In cases of long standing, this may require several weeks; occasionally a large deposit is discovered after the operation and a second operation may be indicated for its removal. This occurred in one of my patients in whom a deposit was discovered in the teres minor muscle about three and one-half months after the removal of three large deposits from the tendon of the supraspinatus. Since this deposit could not be seen in the original roentgenogram, it is believed that it was a recurrence of the trouble.

On the other hand, one or more rather large deposits may be missed at the time of operation. This occurred in the case illustrated in Figure 9. This

patient was relieved by the operation and it is believed that the calcium which was left will be resorbed as a result of the trauma incident to the operation.

SUMMARY

It is noted that localized deposits of calcium occur most often in the musculotendinous cuff of the shoulder but may occur in the vicinity of other joints. The deposits which occur near other joints are similar to those in the shoulder and may be grouped with them.

The etiology, pathology, clinical course, treatment and prognosis of the condition are described.

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DISCUSSION.—DR. FRANK D. DICKSON, Kansas City, Missouri: I should like to add one area in which calcareous deposits occur which Albert Key has not mentioned in his widespread coverage of the body; that is in the tendon of the long head of the triceps muscle. Deposits in the tendon of the long head of the triceps muscle were observed in two ball pitchers who came under my observation, both fast ball pitchers. I think George Bennett will bear me out when I say that fast ball pitchers almost always have shoulder difficulties from degenerative changes, while curved ball pitchers have trouble in the elbow joint. The difference in the distribution of the pathology is due to the different manner in which the ball is delivered in these two styles of pitching.

One young man belonged to an important baseball chain, pitched one game, and was out for the remainder of the season. Examination revealed calcareous deposit in the tendon of the long head of the triceps muscle and a pair of very badly infected tonsils. He was otherwise a very healthy and robust young man, 22 years of age. The tonsils were removed at once, pitching was forbidden, and wheat-germ oil (which I believe contains some form of vitamin C which promotes the absorption of calcium deposits) was administered in full doses. The course of the condition has been followed for three months, and over this period of time the deposits have just about disappeared, and pitching motions can be carried out without pain or discomfort, so it is our opinion that this boy will be able to resume his pitching activities in the spring. The infected tonsils were mentioned because it is my opinion that focal infection does play an important part in formation of these calcareous deposits which are found almost as frequently in women as in men, and in most cases some form of focal infection, usually dental infection, can be unearthed. I must, then, disagree with Doctor Key as to the part played by infection in the formation of calcareous deposits in certain areas of the body, admitting that trauma or wear and tear is usually a factor.

Calcareous deposits in bursae or tendons are incapacitating and usually quite important to the affected individual because of the pain and disability which they produce. It has later been necessary in our experience, however, to resort to surgery. Usually needling of the area or at times irrigation of the area through two good-sized cannulae clears up the situation. If these deposits are irrigated, they usually absorb, probably because of the increased vascularity which follows.

Dr. Edgar L. Gilcreest, San Francisco: Doctor Key covered so much ground that he did not have time to mention a group of lesions of the shoulder that are extra-articular rather than intra-articular, and which are very disabling. We shall forever be indebted to a great anatomist, A. W. Meyer of Stanford, for calling our attention to these lesions in a series of articles in the Archives of Surgery a number of years ago. These lesions should be always held in mind when examining a patient past middle life who has a painful shoulder.

The essayist spoke of conservative treatment and also of surgical intervention. Perhaps we should define these two methods more accurately. By the former is meant, of course, rest and heat to the shoulder; by the latter, an open operation. The point I wish to make is that there is a middle ground between the two, that is, aspirating and needling the bursa. This will often give immediate relief to a patient whose pain has been so intense that he has been unable to sleep for several nights.

Time also did not permit Doctor Key to mention the importance of recovering the function of the shoulder as soon as possible by not permitting contracture of the adductor muscles. These shoulders should be held, so far as possible, in a position of abduction and external rotation. We all see frozen shoulders constantly, due to the fact that this fundamental principle was overlooked by the attending physician or surgeon who has been caring for these patients for weeks or months and, as a result, complete function can never be fully recovered.

I enjoyed Doctor Key's paper very much, as it was most interesting.

Dr. George E. Bennett, Baltimore: One location that I think it would be well for Doctor Key to look over is the junction of the sacrum and the coccyx. I have seen one or two patients who had to be operated on for removal of the deposit at the articulation of the coccyx and the sacrum. Doctor Johnson and I have seen, within the past year, three or four cases of deposits in the biceps, all of which cleared up with conservative treatment.

Dr. Murray M. Copeland, Washington: I have asked (with his acquiescence) to discuss Doctor Key's paper without comment from him about what I have to say, inas-

much as I wish to refrain from stimulating Doctor Key into action with his rapier-like verbal thrusts.

I should like to discuss briefly the use of x-ray therapy in some of the calcified lesions described in Doctor Key's able presentation. There is no great mystery about the use of ionizing radiation. It has been found that x-rays, gamma rays and beta radiation may produce direct nuclear effects in atoms of tissue by collisions. Further, indirect ionizing effects are noted through the ionization of water which makes up a considerable portion of body fluids and tissue. Oxidizing agents and reducing agents are formed in the ionization of water, which may alter the pH of body fluids, the respiration of cells and reduce thrombin, *etc.* With these effects it is not difficult to suggest the possible changes in physiology which occur, including dilation of blood vessels, increased tissue fluid exchange of the part irradiated and, frequently, the resorption of excess salts such as calcium, when present. Increased fibrosis, sclerotic vessels, infection or tissue damage, may retard or prevent favorable therapeutic irradiation effects.

I am not offering these remarks as the ultimate explanation, but I think probably the effects mentioned represent some of the biologic changes brought about by ionizing radiations.

DR. J. ALBERT KEY, St. Louis (closing): I do not like to needle shoulders. You have to get the needle in the calcium in the floor of the bursa, and this may be difficult. When it is in the bursa it means the deposit has ruptured and the contents have become disseminated and pressure has been released. Usually those cases get well promptly if you leave them alone. If you can hit the right area with the needle—usually about a 16 gauge, which is quite a needle—and you jam it around in the area, you may get absorption. My experience has been that those people have a pretty tough time for 48 hours and maybe longer after the needling, before they start to get well, while with a little incision which can be made under local anesthesia, one can clean it out and close up, and when the patient wakes up his pain has gone and he gets well.

PARTIAL HEPATECTOMY WITH INTRAHEPATIC CHOLANGIOJEJUNOSTOMY*

A USEFUL ADDITION TO TECHNICAL METHODS FOR THE MANAGEMENT OF COMMON DUCT STRICTURE

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ONE OF THE MOST DIFFICULT PROBLEMS encountered by the experienced surgeon concerns the repair of a stricture of the common bile duct. Intrahepatic cholangiojejunostomy with partial hepatectomy, a procedure recently introduced by Longmire,[5] is a valuable technic for use in certain unusual and especially difficult types of biliary stricture.

ETIOLOGY AND PREVENTION OF BENIGN STRICTURE OF THE COMMON BILE DUCT

It is well known that benign stricture of the common bile duct may rarely occur as a result of infection in and about the duct. Fibrosis of the ampulla of Vater may result in stricture. The majority of benign strictures of the common duct result from injury to the duct acquired during the course of cholecystectomy. Such injuries are most likely to occur when clamps or sutures are placed blindly in an attempt to control bleeding which may take place during a routine cholecystectomy. Experienced surgeons have repeatedly called attention to the necessity for great care in the management of such problems in order that serious complications may be avoided. The surgeon or first assistant can almost always control such hemorrhage by compression of the hepatic artery between the index finger and thumb after the finger has been inserted into the foramen of Winslow. Adequate light, good retraction and proper anesthesia are, of course, necessary before such a situation can be managed safely.

A number of injuries of the common bile duct have occurred in operations that were considered by the original operator to be technically easy. In such instances, the common duct is usually pulled up, ligated and divided without the knowledge of the operator. Adequate surgical training and constant attention on the part of the surgeon are necessary to decrease the incidence of this distressing complication.

METHODS PREVIOUSLY USED FOR THE REPAIR OF COMMON BILE DUCT STRICTURES

The fact that so many methods of repair have been devised for stricture of the common duct is good evidence that no one method is uniformly successful. It is also true that no one method is applicable to all cases. The methods in use have consisted of variations of two general principles. These are (1) end-to-end suture of the duct and (2) suture of the proximal end of the duct to the

* Read before the Southern Surgical Association, White Sulphur Springs, W. Va., December 8, 1948.

stomach, duodenum or jejunum. Advances have been made in this field, but the problem will long remain a serious one. It is generally agreed that a mucosa-to-mucosa, end-to-end anastomosis of the common duct is the procedure of choice where this can be accomplished. Cattel[1] has been able to accomplish repair by this method in a remarkably high percentage of cases by mobilizing the portion of the distal common duct which lies in a retroduodenal intrapancreatic position. Allen,[2] by popularizing the Roux Y procedure, made

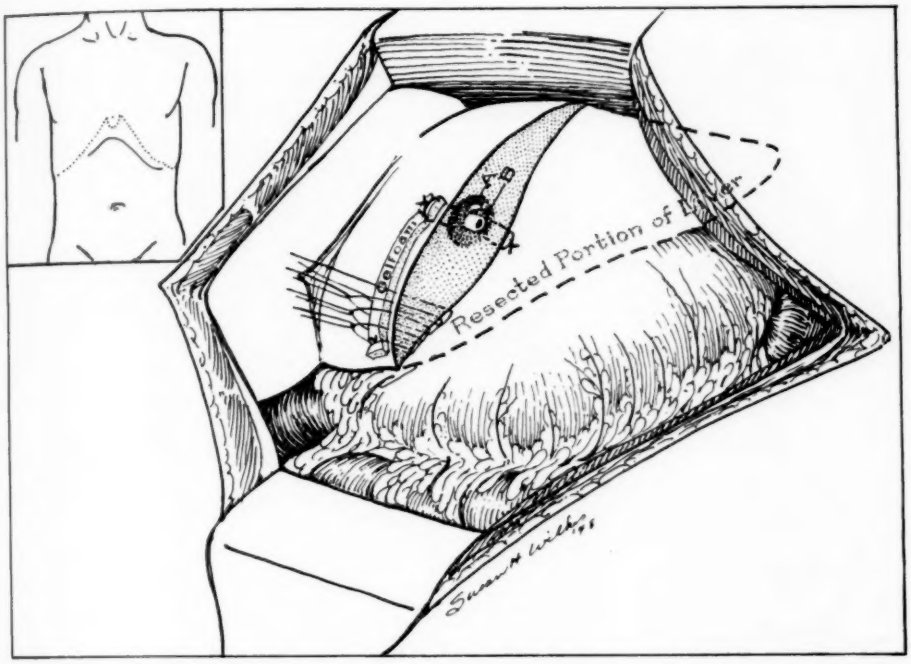

FIG. 1.—Resection of left lobe of liver. Bleeding from the cut liver edge is controlled by utilizing overlapping mattress sutures which are tied over a strip of gelfoam. At the site of the intrahepatic duct one mattress suture is placed through the liver substance above the duct and another is placed through the liver below the duct to avoid inclusion of the duct by mattress suture. An artery (A) which requires individual ligation often accompanies the intrahepatic duct (B). A small amount of liver tissue adjacent to the duct is removed with a curette.

Inset shows incision used. Left lobe of liver is delivered into wound after dividing the triangular ligament.

a definite contribution to the problem. Dragstedt[3] and Zenninger[4] have also made helpful suggestions in the management of such cases.

In an occasional case which has resulted from injury or infection, almost no remnant of the common bile duct may be found. It is in such cases that intrahepatic cholangiojejunostomy with partial hepatectomy may offer the possibility of cure in an otherwise hopeless case.

LONGMIRE PROCEDURE

As a result of studies on human livers obtained at autopsy, Longmire concluded that the left main hepatic duct drains the left lobe of the liver, the

quadrate lobe and most of the caudate lobe. Evidence was also found which suggested that the right and left duct systems might communicate through numerous fine ducts in the caudate lobe. Before the Society of University Surgeons in January, 1948, Longmire reported upon a patient in whom he had successfully performed an anastomosis between the main left hepatic duct and the jejunum after performing a partial hepatectomy to expose the duct. It was pointed out that the dilatation produced by chronic obstruction affords a larger duct for anastomosis than otherwise would be found.

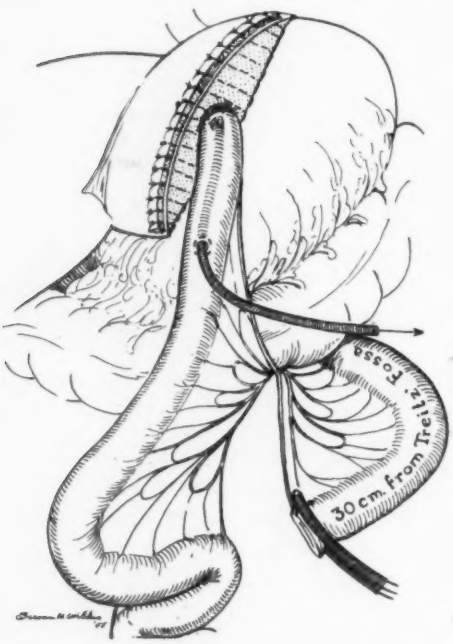

FIG. 2.—The Roux Y is utilized in securing an end-to-end anastomosis between intrahepatic duct and jejunum. The anastomosis is performed around a catheter which is brought out the jejunum by the Witzel method. Interrupted sutures are used in performing the mucosa-to-mucosa, end-to-end anastomosis. The end of the jejunal loop is partially closed on either side prior to performing the anastomosis in order to compensate for the disparity in size of structures to be united.

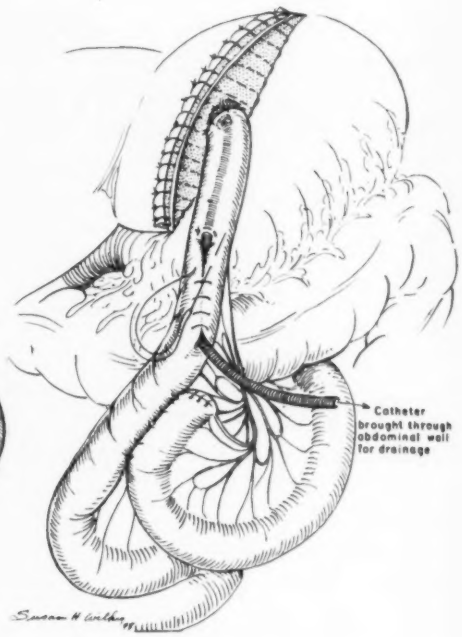

FIG. 3.—After completion of the duct anastomosis the Roux Y is completed and the catheter is brought outside through a stab wound. Penrose drains are also brought out through stab wound.

Case Report: D. M., a 44-year-old white male, entered the hospital on our service January 31, 1948. The patient's chief complaint was jaundice accompanied by recurring bouts of chills and fever.

Sixteen months prior to the time we saw the patient he had undergone cholecystectomy. The gallbladder was said to have contained many stones. The postoperative course was uneventful except for an unusually profuse drainage of bile from the wound for a number of days. Subsequent to his original operation the patient began to experience recurrent attacks of jaundice which varied in intensity. He was hospitalized on three

occasions because of this complaint. On March 21, 1947, the patient underwent an exploratory laparotomy and was told that no obstruction was found in the bile ducts. His condition was not improved by this operation.

The jaundice varied somewhat in intensity but never disappeared. Fever recurred at irregular intervals. The stools were clay colored and there were varied digestive complaints. The patient lost 40 pounds in weight and was forced to give up his work.

Physical examination on admission to our service revealed a debilitated white male who was obviously jaundiced. There was a healed upper right rectus scar. Slight tenderness was noted beneath the right costal margin.

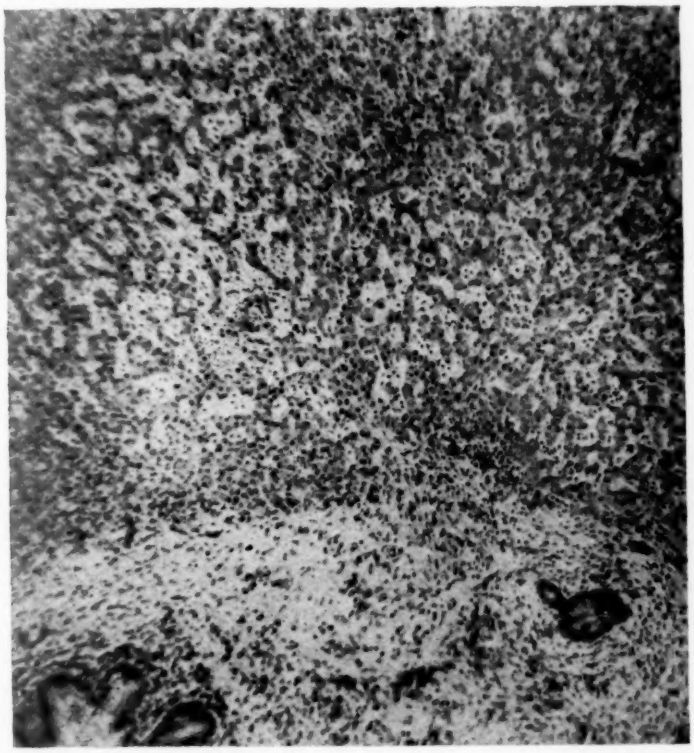

FIG. 4.—Photomicrograph of section of excised liver reveals definite pathologic changes in the liver. There is a pronounced fibrosis in some periportal areas. Round cell and polymorphonuclear leukocyte infiltration indicate presence of hepatitis.

Laboratory studies revealed the presence of bile in the urine and the absence of bile in the stools. The serum bilirubin at this time was 3 mg. per cent and the Van den Bergh reaction was reported as positive direct. The prothrombin time was 20 seconds as compared with a normal control of 40 seconds.

On February 3, 1948, an exploratory laparotomy was done by one of us (C. E. G.). After long and careful dissection with division of many dense adhesions, a diligent search failed to disclose any evidence of a common bile duct, except for a short distal segment which was located behind the duodenum. Three small irregular stones were found in this duct remnant. At the hilus of the liver a small duct approximately 3 mm. in diameter and 2 mm. in length was found making its exit from the liver substance. A small amount

of bile drained from the duct, but we were unable to catheterize this structure. It was decided to perform a hepatoduodenostomy. Accordingly, a small longitudinal incision was made in the superior wall of the duodenum, which had previously been freed by incising the peritoneum along its lateral border. The duodenum was then lifted and the margins of its opening in the superior wall were sutured to the undersurface of the hilus of the liver. This was sutured about the point of exit of the duct from the liver to give the effect of a sort of cup-like container beneath the duct opening.

The patient was not improved by the procedure. The jaundice persisted, as did the recurring attacks of chills and fever. It was our opinion that the Longmire procedure, namely, partial hepatectomy and anastomosis of the bile duct of the left lobe of the liver to the jejunum, was indicated.

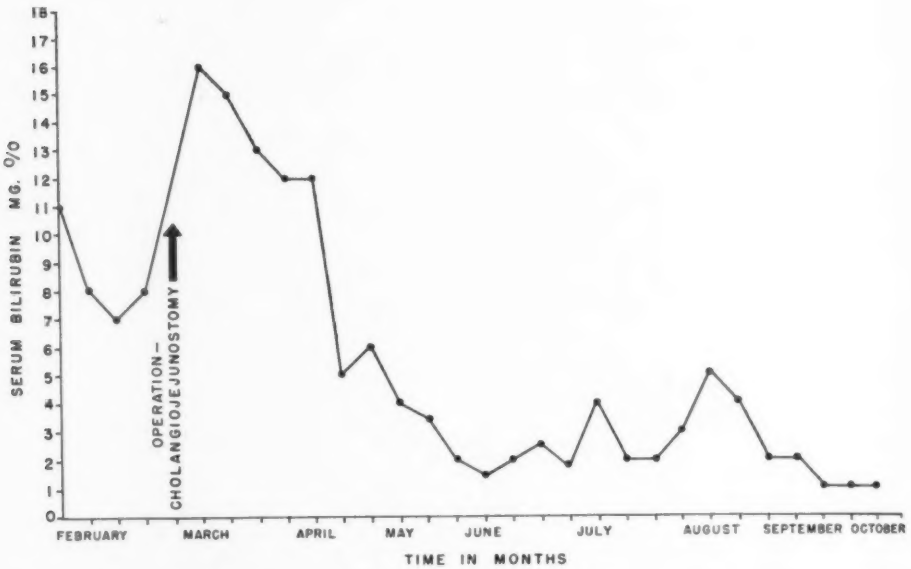

FIG. 5.—Serum bilirubin determinations before and after liver resection and intrahepatic cholangiojejunostomy.

On March 13, 1948, this procedure was accomplished. A modified inverted V type of subcostal incision was used. The triangular ligament supporting the left lobe of the liver was divided and the left lobe of the liver delivered into the wound. The lobe of the liver was compressed between the left index finger and thumb while the partial resection of the liver was accomplished. Through-and-through overlapping mattress sutures were used to control bleeding from the cut surface of the liver.

A bile duct was found of size sufficient to allow the placement within it of a number 14 French catheter. Liver tissue immediately adjacent to the duct was curetted away in order to leave 5 mm. of the duct protruding beyond the cut surface of the liver. A Roux Y loop of jejunum was utilized to make an end-to-end anastomosis between the jejunum and the bile duct. Care was taken to secure an accurate mucosa-to-mucosa anastomosis. The anastomosis was performed over a catheter and the catheter was brought out the jejunum in the Witzel manner.

Microscopic examination of the portion of liver removed showed the presence of a rather diffuse hepatitis. There was an increase in the connective tissue in many of the periportal areas and there was also a rather extensive inflammatory reaction present,

characterized by the presence of infiltration with polymorphonuclear leukocytes and with round cell infiltration.

The immediate postoperative course was a stormy one characterized by fever. A partial wound disruption required secondary closure on the twelfth postoperative day.

Bile was noted in the stool on the third postoperative day and has continued to be present. The patient's general condition has gradually improved and he has gained approximately 20 pounds in weight. The patient states that he feels better than he has since the onset of his original biliary symptoms. He has returned to full time work as a stationary engineer. The serum bilirubin determination has returned to normal.

SUMMARY AND CONCLUSIONS

1. The gravity of common bile duct injuries is emphasized and the commonly used methods of repair are briefly reviewed.

2. No one method of bile duct repair is applicable to all cases.

3. Cholangiojejunostomy with partial hepatectomy offers a method of re-establishing continuity of the biliary tract in some exceptionally difficult cases where restoration of continuity by other methods has heretofore been impossible.

4. One case treated by cholangiojejunostomy and partial hepatectomy is reported.

5. Regardless of the type of treatment used in re-establishing continuity, such patients are subject to the possibility of recurrent difficulty over a period of years.

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DISCUSSION.—DR. FRANK H. LAHEY, Boston: I am sure that it is of value to all who have to deal with stricture cases, to be aware of the various methods that can be used, because anyone who has dealt with many of them will willingly admit that they are difficult, that they are often unsatisfactory and that, no matter what is done, eventually many of them get into trouble again. On the other hand, I believe we should present the results of our experiences to bear out what the author has stated; that is, any method that does not preserve the sphincter is not as good as one that does. It will be impossible in some cases to do an end-to-end anastomosis, as Doctor Cattell and I have tried to bring to everyone's attention. We are not sure whether or not we devised this, and we do not care. We do know that it is not recognized and utilized as a method as often as it should be, and we have urged its use on every occasion when we have discussed this problem.

We want to stress these things again. If a bile duct is injured it is not the common duct in most cases, it is the hepatic, the high hepatic that is injured. This means that that portion of the duct in the pancreas, behind the duodenum, is protected from injury and is

therefore available if it can be found, and it can be found in almost all cases if you know how. I have been unable to find it once or twice, but on at least one occasion when I did not find it, autopsy revealed that it was there and I should have found it. It often takes hours, literally; it takes a tremendous amount of pains and patience, with the bleeding that comes from splitting the head of the pancreas. It takes mobilization of the duodenum. It is difficult, but it can be found, and it can be better found outside the duodenum in most cases than through the duodenum and trying to find the papilla. The papilla within the duodenum is difficult to find; the duodenum bleeds, the papilla is lost in the duodenal folds. You can often come upon it, but if you do not it is difficult to know at what level to make the incision in the duodenum at such a point that it is easy to find.

If you can find that portion of the duct which is in the head of the pancreas, and if you can split the edge of the pancreas, you will remember that the duct is well vascularized by its own blood supply, because it has annoyed you more than once in operating for common duct stones. If you can mobilize it you can mobilize the head of the pancreas, and you can mobilize the duodenum so that you can usually get it up to the end of the cut hepatic duct.

Regarding the operation of anastomosis of the left hepatic duct in the left lobe of the liver to the jejunum, the point I would like to make in connection with this operation—and I have no desire to condemn it or to detract from its originality—is that I believe when the left hepatic duct can be anastomosed to the jejunum by amputating the left lobe of the liver, a good section of common hepatic duct will of necessity remain, to which, with the mobolized common duct, a direct anastomosis can be made and thus preserve the sphincter. We have had Doctor Meissner, who is associated with Dr. Shields Warren in pathology, do a number of corrosion specimens for us, injecting the bile ducts with a plastic material. We believe that the two duct systems are largely separate and, as shown by these corrosion specimens, the left lobe of the liver has a bile system which comes down to the left hepatic duct to join with the right hepatic duct, the right lobe largely having a biliary tree and hepatic duct of its own. We believe there are almost no communicating branches that are of any great value; if there are communicating branches they are small and of relatively little value even, I believe, with dilatation. I would like to make sure that everyone understands this point—that this operation of implanting a left hepatic duct into a jejunum has no advantages over implanting a common hepatic duct into the jejunum, which can be done if common hepatic duct remains, and does have the disadvantage of not making use of the sphincter.

Doctor Cattell has developed a plan for patients who have only the two intrahepatic ducts left, which you will find valuable. I reported at the last meeting of the New England Surgical Society 227—not operations—but 227 patients with stricture of the bile duct upon whom we have operated. These strictures have been of all kinds and the patients have been through all kinds of procedures before coming to us; that series is now around 235. What often makes this operation of duct mobilization and direct anastomosis so difficult in cases in which we would like to employ it, is that the patients have been operated on so many times that the common hepatic duct is completely destroyed. I have just operated on a patient who had been operated on seven times; Doctor Cattell has just sent one home who had eight attempts at repair. In those cases there is no common hepatic duct left; they are all intrahepatic divisions, and in dealing with these stricture cases one must learn to dissect the intrahepatic duct out of the liver with the fulguration apparatus. You have to learn to demonstrate them within the liver as individual ducts. What Doctor Cattell has done that I think is a real contribution, is to approximate the intrahepatic duct divisions by intraductal suture, to convert two ducts to one, split them, and then put a Y-tube up one and a straight tube down the other for anastomosis to the end of the common duct. Many of these are not going to be great successes, but if the sphincter is preserved the patient has a better chance than if it is not preserved.

We know that the Lord will help you on many of these cases. He has to—and everyone knows our golf pro who has been around the clinic so long. We have performed

seven operations on him; he has now gone three years since the last anastomosis, is well and has won several golf tournaments. He has had rubber tubes and vitallium tubes put in and now has a successful direct anastomosis. I plead with everyone not to go through what we went through originally—if it is avoidable, and sometimes it is not; that is, makeshift procedures, such as implanting tubes and anastomosis of hepatic ducts to bowel. We should try to do an operative procedure that offers a chance of getting the patient permanently well, and avoiding if possible ascending infection. All patients with duct anastomosis and tube implantations do not have ascending infection. Some of the jaundice attacks they have are the result of recurrence of stricture. I do not mean to say that end-to-end anastomosis will abolish those; they will occur just the same, but when a good mucosa-to-mucosa anastomosis is obtained it will produce a better result than any of these makeshift procedures.

This is so trite that I blush every time I say it, but we ought to concentrate on giving more attention to publicizing how dangerous cholecystectomy is. We realize that cholecystostomy has been almost abolished, but thousands of cholecystectomies are being done every day and each one is a possible stricture. If the patient died instead of recovering after injury to his ducts, in many cases he would be better off than to live with what he has to go through in the way of expense and suffering. We should publicize the fact that cholecystectomy is a dangerous operation. It is dangerous unless one realizes how important it is to control the blood supply, to demonstrate definitely the anatomic relationship, and to realize that anomalous anatomy is very common. I believe we could do nothing better than to write more and more on the need for accuracy in cholecystectomy, and recording the finding of the common duct in the pancreas and behind the duodenum.

I believe that many tend to say—"Oh, I cannot find that duct in all that scar tissue." You can. If you will lift the head of the pancreas where it projects to the right beyond the duodenum, if you will mobilize the edge of the duodenum by freeing the vascular external edge that bleeds so and annoys you, and roll it in, you can find it if you are patient. Then if you find the common duct in the head of the pancreas you can mobilize it, and you can put the ends of the common and hepatic ducts together in many of the cases. It is surprising how much duct is left when you have exposed it. You must remember that the duct does not go straight down; it goes over and then down, and when it is freed it becomes straight. In many cases these ducts can be put together up in the hilum of the liver. If a T-tube is inserted it must be left in a minimum of a year; it must not go through the anastomosis but in a slit below, with the upper limb up through the anastomosis. It must be irrigated daily or night and morning, or it will block; it will occasionally need ether injections. If left in for a year, in many instances the results will last and will be better than those obtained with other methods.

I would not have you think that we say this operation can be done on every case because we know that is not so, but I do want to say that with experience you will be surprised how often you can find a good length of the duct and how often you can put the two ends together which, after all, is the most physiologic of all operations for stricture of the bile ducts.

DR. R. L. SANDERS, Memphis: It is a pleasure to discuss this paper, particularly since it was presented by one of our younger surgeons on his first appearance before this Association. Doctor Longmire, who originated the operation described, and Doctor Wilson have both recently become professors of surgery, Doctor Longmire at the University of California and Doctor Wilson at the University of Tennessee, and both are to be congratulated on the fine work they are doing.

Doctor Lahey has just expressed much of what I wanted to say. Every surgeon will agree that, if possible, defects of the ducts should be repaired by end-to-end anastomosis. Occasionally, one encounters a case, such as that reported by Doctor Wilson, wherein the duct has been destroyed so completely that nothing remains to bridge the wide gap between the liver and the pancreas.

We recently had a case similar to that of Doctor Wilson, which I reported just last week before the Western Surgical Association. The patient, a lady 32 years of age, had had a cholecystectomy elsewhere and at the operation both the common and the hepatic ducts had been excised. A short time later she had become jaundiced and a tube had been inserted for drainage. At her first visit to us, 8 months postoperatively, the tube was draining bile-stained fluid, but she was still jaundiced, was having chills and fever, her liver was enlarged, and she had lost 20 pounds in weight. On exploration we could find only a short end of the duct down beneath the head of the pancreas. The proximal end had sloughed away up into the liver hilus and completely strictured, producing a bile cyst. After evacuation of the cyst, an hepaticojejunostomy was performed according to the Allen method. The operation was successful for a time. Eight months later, however, the patient returned, presenting the same clinical picture as before. We operated again, this time disconnecting the jejunum at the hilus, removing a large number of stones from a pocket in the liver and, since no duct could be found, resuturing the end of the jejunum into the liver hilus. The mucosa was not inverted, in the hope that by this measure the anastomosis might be successful. As before, the suture was made around a tube which was brought out through the jejunum below. The patient progressed satisfactorily for six weeks. The chills, fever and jaundice then recurred and were accompanied by abdominal pain and the passage of blood through the bowel. The liver was enormously enlarged. Despite medical treatment, her condition grew worse and it became apparent that something drastic must be done. Having in mind Doctor Longmire's operation, and with the inspiration of Doctor Wilson's success in the case just reported, I decided to try a similar procedure.

On exploration, the left lobe of the liver filled the upper abdomen, displacing the right lobe to the other side, and was in such poor condition that removal of the entire lobe seemed advisable. Before its removal, through-and-through mattress sutures were inserted along the dividing line between the lobes to control hemorrhage and, after removal, continuous sutures were inserted along the cut edge. The left hepatic duct was isolated for a distance of two inches as the lobe was being removed. An attempt was now made to draw up the common duct for anastomosis to this segment, but was unsuccessful. The jejunum proximal to the Roux-Y anastomosis formerly made was therefore brought through the transverse mesocolon and the side united to the end of the hepatic duct, mucosa being sutured to mucosa. A lateral enteroenterostomy was then made below. Finally, as a precaution against slipping, the jejunum was tacked to the under surface of the liver for some distance on both sides of the anastomosis with the duct, and to the transverse mesocolon at its point of emergence. The previously made hepaticojejunostomy was not disturbed.

To the present time, now more than six months postoperatively, the patient has been getting along well and has gained 35 pounds in weight. Her icterus index is still elevated, but the liver is decreasing in size. It is probable that, sooner or later, the duct will restricture; even so, the operation will have been worth while.

As stated in the beginning, such procedures as these should be employed only after every effort has been made to unite the two ends of the damaged ducts. When the occasion does arise, however, they may offer the solution, at least for a time, to the patient's serious predicament.

Dr. Waltman Walters, Rochester, Minn.: I think we should congratulate Doctor Wilson and also Doctor Sanders, for putting to clinical application an experimental problem which Doctor Longmire worked out so well in Doctor Blalock's laboratory. It seems to me this is the very best type of investigation, in which we all should be interested. I have had on another occasion an opportunity to congratulate Doctor Blalock on the clinical application of certain fundamental principles which he and his associates have studied in the experimental laboratory and have then carried into the field of clinical

surgery. I think the presentation of these two cases today by Doctor Wilson and Doctor Sanders is really an epoch-making occasion and I want to congratulate them both.

These are two or three points one could well consider, particularly in Doctor Sanders' case, in understanding the excellent results Doctor Wilson has obtained. With left partial hepatectomy and hepaticoenterostomy it stands to reason that there must be some collateral circulation between the ducts in the left lobe and in the right lobe, for if there were not, after the passage of the sixth month Doctor Sanders' patient would have continued to be jaundiced. Regardless of what the corrosion specimens show, and these were thoroughly studied 22 years ago by McIndoe and Counseller, there is no doubt that there is a communication between the two lobes of the liver, through their main hepatic duct when these ducts unite within the liver, as they do in most cases. Moreover, the possibilities are that, when obstruction occurs in the extrahepatic bile ducts, there is a greater tendency for an intercommunication than there would be under normal circumstances. I believe that is one reason why, if one is successful, as these gentlemen have been, with this procedure, there is reason to believe there may be sufficient communication between the two sides of the liver so that it will work effectively. I do not believe either Doctor Wilson or Doctor Sanders need be too pessimistic about future results; after all, if one can relieve the patient of a very serious condition in which there is serious damage to the liver, even if it be necessary later to do a somewhat similar operation or a variable one, I think a great deal has been accomplished.

I want to congratulate both these gentlemen for making a very fine contribution to surgery, and I also want to congratulate some of the younger surgeons who are doing experimental work, Doctor Blalock and his associates, Doctor Longmire and others who have applied clinically the principles which these gentlemen have learned in training young American surgeons.

DR. HARWELL WILSON, Memphis (closing): Doctor Longmire, with whom I have discussed this problem, feels very definitely that, as Doctor Walters intimated, there is a definite communication between the right and left lobes through the caudate and quadrate lobes. In addition to making this statement, I would like to thank Doctor Lahey, Doctor Sanders and Doctor Walters for their discussions.

COMBINED SUPRADUODENAL AND TRANSDUODENAL EXPLORATION OF THE COMMON BILE DUCT*

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THE OBJECTIVES of this presentation are to discuss the advisability of opening the duodenum at the time the common bile duct is explored; to present as evidence a group of cases to show that combined supraduodenal and transduodenal exploration of the duct at the same time offers certain distinct advantages over and above those obtained by only supraduodenal exploration of the common duct; and to show advantages gained by extending the T-tube draining the common duct into the duodenum.

A brief recapitulation of the important steps in the development of surgery for benign lesions affecting the common bile duct may be interesting. The operation of opening the common duct above the duodenum for the removal of stone was first performed by Kümmell,[11] who described the procedure in 1890, and by Thornton[17] who first successfully performed the operation in 1889 and reported it in 1891. The procedure of removal of stones by incising the duct in its retroduodenal portion has been credited to Haasler,[9] who described it in 1898. McBurney[14] performed a transduodenal operation first in 1892. McBurney opened the duodenum, severed the ampulla and removed the stone, but he did not open the common duct above the duodenum. In 1898, he reported six cases with five recoveries. Kocher first performed a transduodenal operation in 1894. He cut through the duodenal mucosa into the common duct but did not sever the sphincter. The common duct and duodenal walls were approximated with sutures.

It is difficult to find in the literature the basis for the frequently expressed extreme aversion to opening the duodenum to obviate obstructions of the common bile duct. Undoubtedly it may be attributed to fear surgeons have of duodenal fistula and of the danger of infection and peritonitis. Another factor in their attitude may be the feeling that duodenal reflux or regurgitation of duodenal contents into the biliary tract can set up cholangitis and fatal infection in a high percentage of cases.

However, it is time for a new evaluation of the dangers of opening the duodenum with present technical methods and under modern chemotherapeutic measures. When the duodenum is opened for the exploration it should be carefully mobilized; the superior leaf of the transverse mesocolon should be cut and pushed back. A longitudinal incision in the descending portion of the duodenum should be closed transversely, securely and carefully. I prefer running fine chromic catgut for an inner suture and interrupted silk for the outer.

* Read before the Southern Surgical Association, White Sulphur Springs, W. Va., December 8, 1948.

If the duodenum has been mobilized, secure closure more readily may be effected.

Duodenal reflux may not be so dangerous as it has been regarded. Whether it often causes symptoms may be debatable. I have left tubes in the common duct anastomosed to the jejunum after pancreatectomy for months before removing them and cholangitis did not result. Moreover, in those patients in whom we have pulled the end of the T-tube through the papilla into the duodenum after choledochotomy, no symptoms of cholangitis resulted.

The almost universally accepted method of releasing benign obstructions of the common duct is to open the common duct above the duodenum, and

FIG. 1.—Examples of extension of common duct drainage tubes into the duodenum as illustrated by postoperative cholangiograms. The transvaterian extension of the tube prevents the recurrence of stenosis at the duodenal opening of the common duct.

remove such stones as may be engaged with forceps or scoops, by aspiration and lavage of the ducts and by passing graded dilators (Bakês dilators) through the ampulla of Vater into the duodenum. Some surgeons question the advisability of forcefully dilating the lower end of the common duct and the ampulla with Bakês dilators.

Practically all surgeons in this country apparently feel that the best method of managing the common duct after it has been opened is to place a T-tube in it with short transverse limbs, so that "it can be easily removed" and so that the tube does not extend into the duodenum. Apparently one of the objections to passing the tube into the duodenum is the fear of permitting duodenal contents to regurgitate into the biliary system. To this attitude, and I believe to his credit, there is one man who has taken exception, and that is Richard Cattell, who has devised a long transverse limb common duct tube with the expressed intention of having one arm of the tube extend through the

common duct into the duodenum and even into the jejunum. Apparently the advantages to be gained by this have not been readily seen and accepted by surgeons in general. For there yet fails to be one authoritative article endorsing his tube and the idea, and many surgeons continue to show in postoperative cholangiograms short-arm T-tubes inserted in the common duct with definite or questionable filling defects.

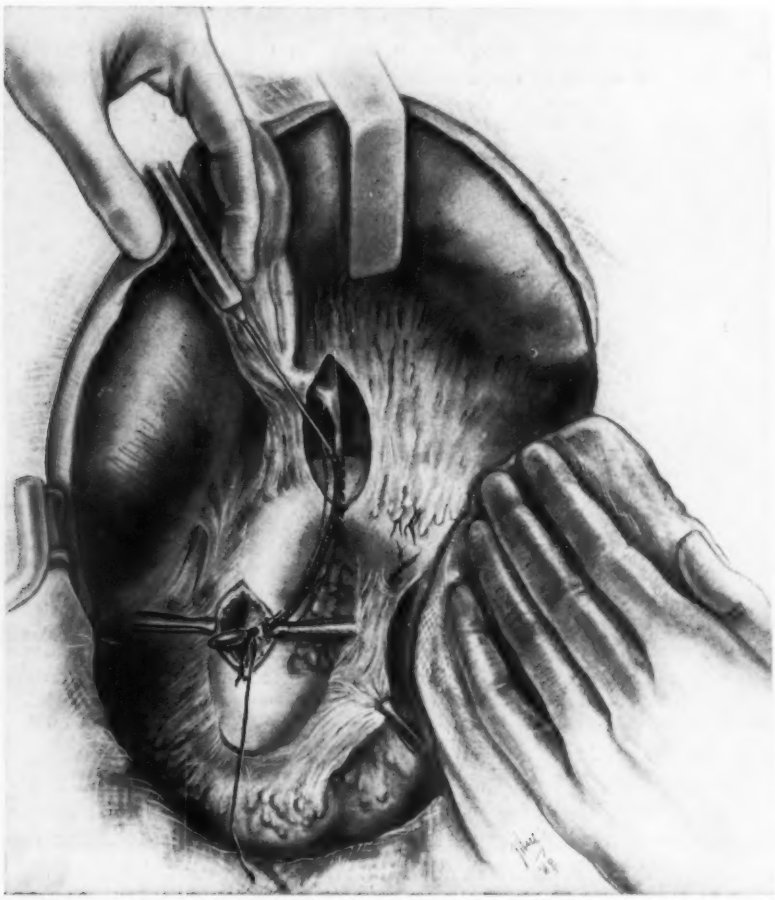

FIG. 2.—Illustrating method described in text of combined supraduodenal and transduodenal exploration of the common duct. In order to facilitate the introduction of the common duct T-tube and insure the passage of its lower arm into the duodenum a piece of silk is tied onto the Bakes dilator and is withdrawn through the common duct.

On my private services I have opened the duodenum and the supraduodenal portion of the common duct in 16 cases when exploring the common duct. This is admittedly a relatively small group of patients. Even in this small number information has been obtained which has really surprised us. No death resulted in this group of patients. Instead of using shortened transverse T-tube arms which would remain in the vicinity of the opening to drain the

supraduodenal portion of the duct I have left one arm long and have deliberately pulled it into the duodenum, having the T-tube jut beyond the ampulla of Vater. Usually an ordinary T-tube is employed. Occasionally these are too short and a Cattell tube is used. This will prevent the recurrence of stenosis if the tube is left in for a sufficient length of time.

Stones were found in 11 cases and stenosis of the ampulla of Vater, or the lower end of the common duct, was found in four. A false impression was

FIG. 3.—After the Bakês dilator is withdrawn the silk threaded thus through the common duct is attached to the uncut horizontal limb of the common duct T-tube and the tube is drawn into the duodenum.

gained in three instances that the probe had traversed the papilla when it actually had not. In three patients a Bakês dilator introduced through the supraduodenal opening of the duct and felt through the duodenal wall as apparently in the duodenum, was ascertained, after opening the duodenum, to be still in the ampullary portion of the common duct and had not come

through the opening in the papilla which was definitely stenosed. When there is little or no inflammatory reaction or edema in the region of the common duct the pancreas is quite mobile, and with a small Bakês dilator it is possible by feeling through the unopened duodenal wall the point of the dilator, to gain the impression that it is actually in the duodenal lumen, when such is not the case. Such a false impression may be one factor in the recurrence or persistence of benign obstructions of the common duct.

TABLE I.—*Operations Primarily for Benign Lesions of the Biliary System*

Cases	78
Cholecystectomy (without exploration common duct)	56
Cholecystectomy (and exploration duct 26%)	20
Exploration duct without cholecystectomy	2
(During gastrectomy, 1)	
(Duodenal diverticulum, 1)	
Duct explored, duodenum opened	16
Duct explored, duodenum not opened	6
Jaundice	14
Jaundice from stenosis (no stones)	3
Stones common duct	14
Stones common duct; no jaundice	3
Death (1) supraduodenal (only) exploration duct	

Stenosis (once with a duodenal diverticulum near the opening of the common duct) was found in four instances. By stenosis is meant a contracture at the opening of the duct into the duodenum which will not pass a 3-millimeter dilator without undue force or cutting the papilla. Perhaps stenosis may explain the high percentage of cases in reported series in which stones are known to be accidentally left in the common duct or reformed after supraduodenal exploration of the common duct had been performed. Certainly many

TABLE II.—*Duodenum Opened (During Common Duct Exploration) 16 Cases*

Unexpected findings	
Stenosis at papilla of Vater	3
(Bakês dilator failed to pass into duodenum)	
Inflammatory mass region of ampulla	1
Passage of residual stones	1
Papilloma papilla of Vater	1
(Stones in common duct)	
Stone in head of pancreas	1
Duodenal reflux	3

of the cholangiograms which are shown in an effort to demonstrate absence of stones or presence of stones after operation show a very decided partial obstruction at the ampulla. Possibly this is ampullary contraction but it may also be stenosis which would be disclosed by the combined operation. In those instances where severe stenosis was found in our cases the ampulla was cut.

We found other surprising conditions when the duodenum was opened which had we not opened it might have been overlooked. In one instance a hard inflammatory lesion of the duodenal wall was found near the ampulla of Vater

causing stenosis. In another instance a patient who had been explored at a renowned institution elsewhere twice within the last three years and stones removed, came to us with recurrent common duct obstruction. We also removed stones through a supraduodenal opening in the common duct, but on opening the duodenum we found a large papilloma, soft and easily overlooked unless the duodenum had been opened and affecting the ampulla of

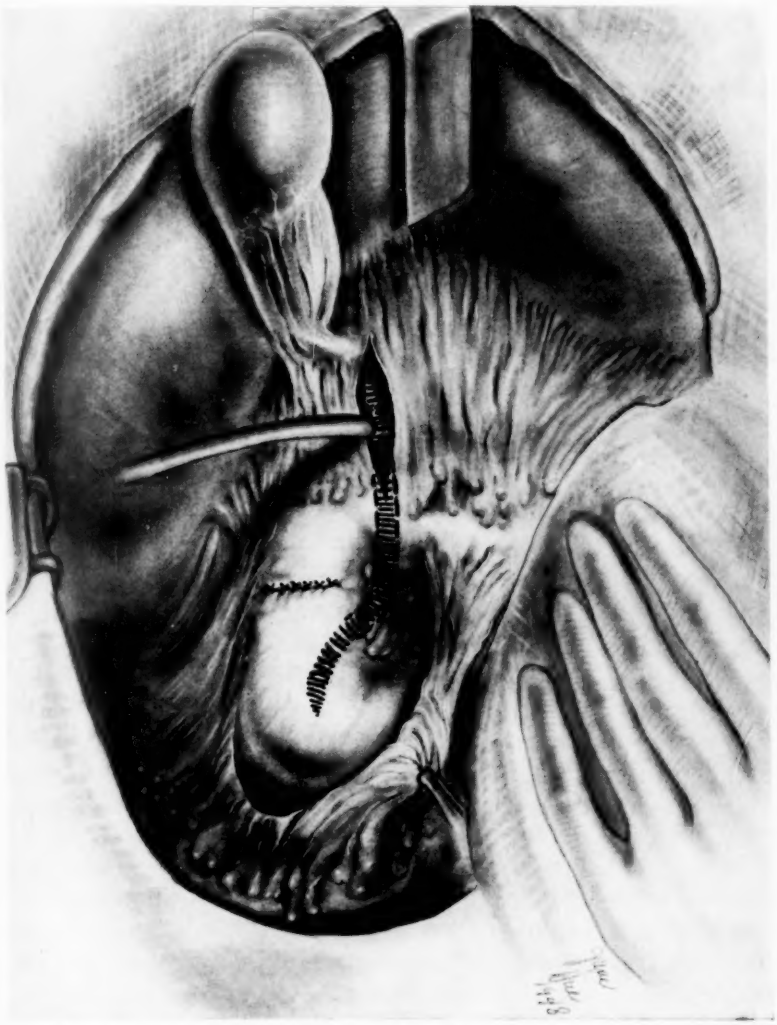

FIG. 4.—After the T-tube is placed in the common duct the supraduodenal opening is closed around the T-tube. The duodenal opening is closed transversely and with care to obtain security. The gallbladder is then removed.

Vater. This was removed; the common duct was transplanted into the superior surface of the duodenum and the upper end of the residual intrapancreatic portion of the common duct was closed off by inverting sutures. Because the patient's condition was such that he could not stand pancreatec-

tomy at the time, it has been deferred until he can gain a little more strength. This is a recent case. The patient recovered and has returned to his home in another city. He has gained weight and strength. Another operation will be done in the near future with intention of removing the remaining lower portion of the common bile duct.

In two instances the Bakes dilator made false openings around the stone, once through the pancreas and once through the common duct into the duodenum above the ampulla of Vater. In each instance the stone was removed by transduodenal approach combined with the supraduodenal approach and the patient recovered. In one instance, we have reason to believe that we left three calculi in the common duct. This patient had had a combined supra- and transduodenal exposure and an ampullotomy for numerous stones contained in the gallbladder and common duct. Postoperative roentgenograms showed shadows which we believed to be stones in the common duct. Subsequent studies showed the disappearance of these stones. We believe that they were passed into the duodenum due to the fact that the lower end of the common duct was widely opened.

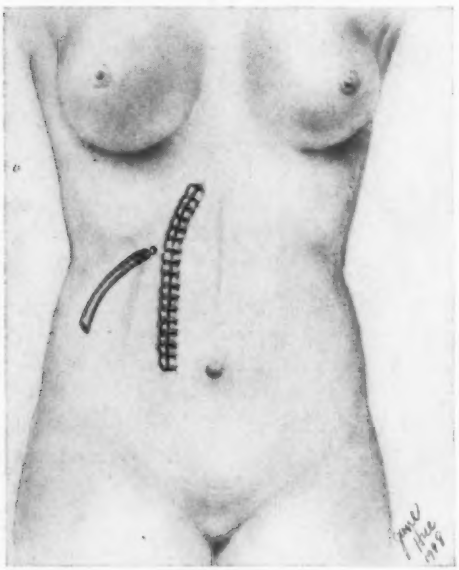

FIG. 5.—After exploration of the common duct super- and transduodenally and removal of the gallbladder the area is lavaged with saline and the common duct tube and a Penrose drain are brought through a separate small subcostal wound.

We have encountered reflux of duodenal drainage, not only through the tube in a number of instances (in almost all cases this may be obtained by suction), but also around the tube in three instances in which it was very severe. All of these patients recovered. It is undoubtedly undesirable to have this as a complication, but it is also undoubtedly not nearly so dangerous as it has seemed to be regarded by surgeons in general.

These 16 cases of supra- and transduodenal choledochotomy occurred in a group of 78 primary operations on the gallbladder and the bile ducts. By primary operation is meant operations directed to the biliary system itself and not to gastric or small intestine or other lesions. Moreover these cases only include nonmalignant lesions.* In this group cholecystectomy has been performed alone in 56 cases, cholecystectomy and exploration of the common duct in 20 cases. Thus the common duct was explored in 26 per cent of the

* Two exceptions, papilloma of the ampulla (because he had stones) and 1 gastric resection where the common duct was intubed by supraduodenal and transduodenal approach.

cases. Exploration of the duct without cholecystectomy was done twice, once because the duct was intubed during a gastrectomy for ulcer which had penetrated onto the head of the pancreas and once for operation for duodenal diverticulum.

There was one death in the entire series of 78 cases, and this occurred in a patient who had cholecystitis and cholelithiasis, choledocholithiasis and hepatitis. We operated upon him under unfavorable conditions and when he had high fever, feeling that his condition was deteriorating and that we must hasten to give him a chance of survival. The supraduodenal portion only of the common duct was opened, stones were removed and a T-tube was placed in the common duct. The gallbladder was removed. Another patient in which a cholecystectomy was done during the course of an operation which was performed for resection of jejunum for diverticula, died. The judgment at operation was that cholecystectomy would add little to the risk and it was done. The patient died of peritonitis. This case is not included because it is not considered an operation primarily directed to benign lesions of the biliary system. The major problem was of another character. Another case is excluded in which a cholecystostomy was done but the operation was performed for filling defect, (polyposis) of the stomach in an 80-year-old woman. In two instances, in addition to the above, we removed the gallbladder for carcinoma, once in conjunction with resection of the transverse colon onto which the carcinoma had spread. Both of these patients recovered.

SUMMARY

A group of cases is reported in which the exploration of the common duct was carried out both supraduodenally and transduodenally. There were no deaths from the 16 operations. Simultaneous supra- and transduodenal exploration of the common duct revealed at times unexpected pathologic findings, such as stenosis of the ampulla of Vater, unexpected neoplastic and inflammatory lesions of the ampulla, residual stones in the lower end of the common duct. The duodenum may be opened without an appreciable increase in risk to the patient and it probably insures the surgeon and patient against persistence of conditions which primarily led to the formation of stones in the common duct.

Routine intubation of the common duct with a T-tube following exploration, always with the lower end of the tube traversing the opening in the papilla and entering the duodenum is advocated. This will tend to keep the ampulla open and prevent recurrence of stenosis if it has been present. It is an additional safety factor to permit the passage of small stones when the tube is removed because of the widely dilated papilla of Vater. The dangers which have been attributed to duodenal reflux probably have been in the past greatly exaggerated.

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Discussion.—Dr. William F. Rienhoff, Jr., Baltimore: I have enjoyed Doctor Mahorner's presentation very much and heartily subscribe to his idea of transduodenal removal of gallstones which are impacted in the ampulla of Vater. It has been our custom to make a small incision in the anterior wall of the duodenum parallel with its long axis and over the area in which the impacted stone is palpable. The duodenum once opened, the impacted stone at the ampulla may be delivered up into the wound without difficulty, and incision made in the ampulla with subsequent delivery of the stone. Also, any stones which remain in the common duct may be milked down with great ease. It has often occurred to me that this might be the method to be preferred for removal of a stone of the common duct, rather than opening the duct above the duodenum.

The technic I have employed in closure has been to suture the mucosa of the common duct about the duodenal mucosa through the entire thickness of the wall of the duodenum with interrupted "o" catgut sutures. The incision in the anterior wall of the duodenum is then closed in the opposite direction as in a Heineke-Mikulicz operation.

With regard to drainage of the common duct with a rubber tube for the ordinary run-of-the-mill case of common duct stone, to be differentiated from those cases in which the common bile ducts are full of smudge or bile stone mud, it has been our custom for the past 20 years to avoid placing a tube of any type in the common duct. In 1919, when the late William S. Halsted was recovering from the first operation on his common duct for removal of a common duct stone (which operation was performed by R. H. Follis, Sr.), a T-tube was inserted into the common duct. At that time I was medical interne on the service of Dr. Thomas R. Boggs, who was Doctor Halsted's physician. After removal of the T-tube, drainage of bile persisted for a long period, and Doctor Halsted's

interest in drainage of the common duct was vigorously renewed. It is to be remembered that his first interest in drainage of the common duct began, I believe, when he performed the operation for the first time on his mother in Albany, New York, at which time he removed a common duct stone.

It was realized by Doctor Halsted and Doctor Finney, Sr., that the use of the T-tube in draining the common duct was not only an impractical method, but that when the tube, regardless of how the T was constructed, was removed, the suture line in the common duct was damaged to a greater or lesser degree. This was due to pulling out the tube, which was placed in the duct in those days, through the incision that had been made to remove the stone. The disparity of the opening in the duct and the size of the drainage tube was corrected by means of suturing the incision in the duct about the tube.

After joining the surgical service it was my opportunity to assist Doctor Finney, Sr., for a number of years, and it was he who first suggested closing the opening in the common duct and placing a drainage tube in the cystic duct if the latter were large enough; or, inserting a tube through a separate small opening cephalward, above the original suture line. As a rule, this secondary incision would be made at about the junction of the common hepatic duct and cystic duct to form the common duct. In this manner, a catheter inserted into the common hepatic duct through a separate incision, or one inserted into the cystic duct, could be removed without disturbance, by pulling the suture line in the common duct. This was first employed by Doctor Finney, Sr., and later, at the suggestion of Doctor Halsted, Dr. Mont Reid operated on a number of cases, draining the common duct via the cystic duct, or through a separate small opening in the common hepatic duct if the cystic duct was too small to receive a catheter.

Later, in 1923, when I began my residency in surgery, I discussed drainage of the common duct many times with Doctor Finney, Sr. It was decided to abandon drainage of the common duct in all cases of common duct stone, except those in which there was bile stone smudge or mud present. The technic employed was to open the common duct just above the duodenum, remove the stone or stones, and then insert a uterine sound through the common duct and the ampulla of Vater into the duodenum to be sure that the tract was clear. By this method the sphincter of Oddi was of course dilated in a manner similar to that following dilation of the external sphincter ani, and remained flaccid for some unknown period following dilation. No particular dilators were ever employed, the uterine sound being of standard size which traumatized the ampulla least of any instrument that could be passed through it to assure one of its patency. The opening in the common duct was then closed with interrupted fine silk sutures. The abdomen was always drained with two protective cigarette drains.

For a period of 20 years, with few exceptions, the common duct has been closed in this manner. There is always some drainage of bile-stained serum for four to six days after operation, just as one would expect after simple removal of the gallbladder. There has not been a single instance of any complication resulting from closing the duct without placing a tube within it, and the convalescence of the patient has been much more comfortable, more physiologic and more rapid than if the bile were drained to the exterior through a tube. The dilated ampulla, even though this dilation is slight, allows the bile to proceed along its natural channel into the small intestine, and elderly patients particularly have a much less serious postoperative course. I am opposed to placing a tube in the common duct except under the conditions mentioned above, and I can see no necessity whatsoever for this drainage except in the presence of bile-stained smudge and never, in my opinion, should a tube be used in the ordinary type of common duct stone or stones encountered.

The argument is often used that if a stone is overlooked for some reason and left in the common duct it is better to have a T-tube within it, but this fails to be impressive because, as everyone knows, the stone cannot be removed through the T-tube and the patient will require re-operation in any event. Tubes carry infection, as all drainage tubes do, thereby subjecting the patient not only to the hazard of the infected wound, but

to the more serious problem of infected ducts with a greater or lesser degree of hepatitis.

In the cases of reconstruction of the common duct which I have performed, in which it was possible to do either an anastomosis between the stump of the common hepatic duct and the duodenum or jejunum, or an end-to-end anastomosis between the common duct and the common hepatic duct, I have always placed an indwelling catheter running down into the duodenum. In some cases, depending on the length of the catheter in the duodenum, the tubes have been passed by rectum from two months to three years afterward, and in all cases the lumen of the tube has been completely filled with debris and bile salts which have been precipitated in the tube. The tube has served only as a scaffold and in no sense of the word as an actual canal.

It seems to me that, after these many years and the profusion of papers that have been written on drainage of the common duct, it is time the lack of necessity of placing a tube in the common duct should be brought before this Association.

APPLICATION OF TECHNICS OF RECONSTRUCTIVE SURGERY TO CERTAIN PROBLEMS IN GENERAL SURGERY*

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Galveston, Texas

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It is our firm conviction that reconstructive and general surgery should not be entirely divorced from each other as specialties. The plastic man loses much of the thrill of speculative diagnosis and the satisfaction which follows successful operations in matters of "life and death." If he has had no training in the basic sciences and in the fundamental principles of general surgery, moreover, the scope of his practice is extremely limited. He is apt to become a mere technician with his work confined within the rather narrow bounds of what is popularly known as cosmetic surgery. The general surgeon, on the other hand, misses the stimulation associated with the devising of reconstructive procedures to meet the needs of each individual case as it presents itself. He is deprived, as well, of the pleasure of being able to achieve results which are readily visible and which are of such great emotional and economic importance to the patient.

There are certain plastic principles which are equally useful in all types of "surface" operations and which should be included in the training of every young surgeon no matter what his specialty. First among these may be mentioned the correct placing of incisions to produce inconspicuous scars and to avoid postoperative contractures. In this connection it might be well to serve warning that many textbooks of surgery in discussing this problem use illustrations of Langer's lines of skin tension with vertical markings on the forehead, neck, cubital and popliteal spaces. The proper direction of skin incisions, however, is perpendicular to the action of the underlying muscles in areas where they are attached to the skin, as in the face. Where there is no attachment to the skin, incisions should be placed perpendicular to the direction of excursion of the skin which is produced by normal muscle pull. The most reliable guides are the normal creases of the skin whenever they can be employed. On the face, the shadow lines near the hair margins and the outline of the jaw often prove useful. In the cheek region or other area where it is impossible to follow a normal skin fold, incisions should be staggered to break up the scar line, which would otherwise catch the light and seem more prominent. The practice of making perpendicular incisions in the axilla and across joint creases, where the development of contractures is inevitable, is most deplorable but unfortunately all too common.

In the treatment of traumatic wounds, emphasis should be placed upon the importance of covering all raw areas at the time when the patient is first seen

* Read before the Southern Surgical Association, White Sulphur Springs, W. Va., December 8, 1948.

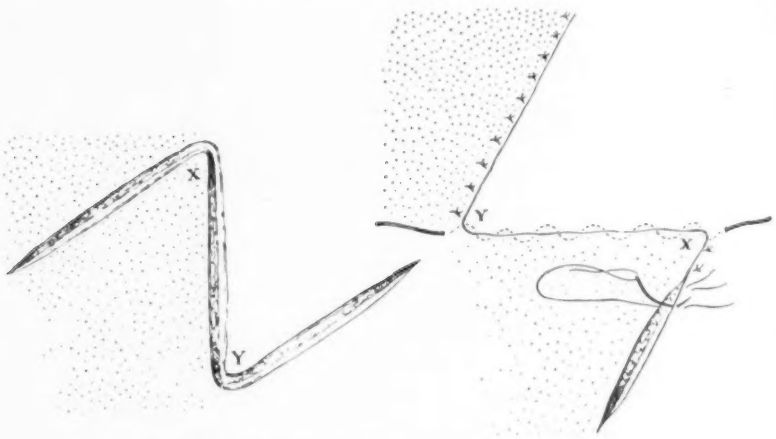

FIG. 1.—Diagram of the conventional Z plastic.

unless lacerations are so contaminated that primary closure is too great a hazard. If the tissues cannot be closed otherwise, a temporary thick-split skin graft may be applied; in the case of an avulsion wound of the hand, a direct flap may be constructed by burying the injured part into the opposite arm or the abdominal wall. The same principle of covering denuded areas as quickly as feasible applies to acute burns, where every effort should be made to prepare patients for at least preliminary grafting by the end of the third week with the use of pressure dressings, adequate chemotherapy and maintenance of normal blood volume and protein balance by repeated transfusions of whole blood.

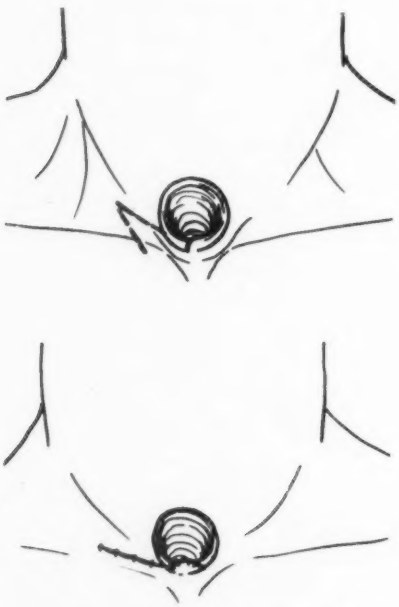

FIG. 2.—Diagram showing the application of a triangular flap in a permanent tracheotomy opening.

It is often a temptation on the part of the surgical house staff, especially when confronted with a number of severe lacerations in accident cases at night, to sew up wounds as rapidly as possible with whatever suture material is at hand. Unfortunately, it is sometimes impossible to remove entirely at a later date a disfiguring scar or the marks of widely placed sutures which might have been avoided with a little patience and care. All wounds should be closed accurately in layers. On the face and exposed surfaces, delicate suture material should be employed; stainless-steel wire gives rise to a minimum of local tissue reaction, and the results obtained with its use are well worth the additional time and effort required.

A pressure dressing should be applied in every case, as a matter of routine, to prevent postoperative edema and hematoma formation.

Sufficient stress should be placed upon the necessity of undermining the surrounding skin to relieve tension on wound edges. If undermining alone is not sufficient, the tissues may be rearranged by the transposition of flaps of skin. The so-called Z-plastic operation, which has been popularized in this country particularly by John Staige Davis, Kitlowski and Ferris Smith, is one of the most useful procedures which the general surgeon may appropriate from the armamentarium of the plastic surgeon. Figure 1 shows the general plan of the Z. Its underlying principle is the achievement of relaxation of the tissues along the central line as a result of the transposition of tissues from the margins of the area into the region of contracture or tension. The central limb serves as a common side of two triangular flaps. The two arms of the Z or reversed Z, as the case may be, are outlined usually at an angle of 60 degrees and blunted to avoid compromise of the circulation at the tips.

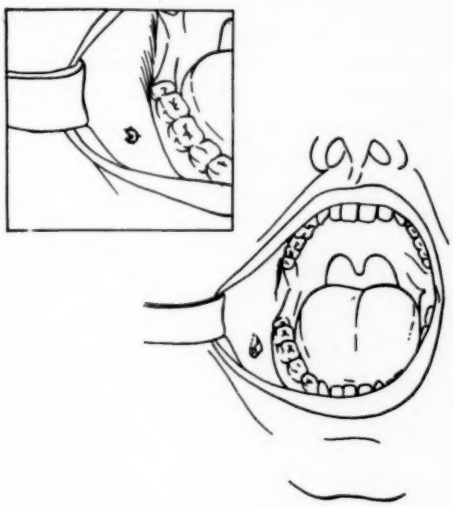

FIG. 3.—Diagram showing the use of a triangular flap in the repair of a parotid-duct fistula.

The contribution of technics of reconstructive surgery to general surgery we feel should not be limited, however, to those which we have just outlined,

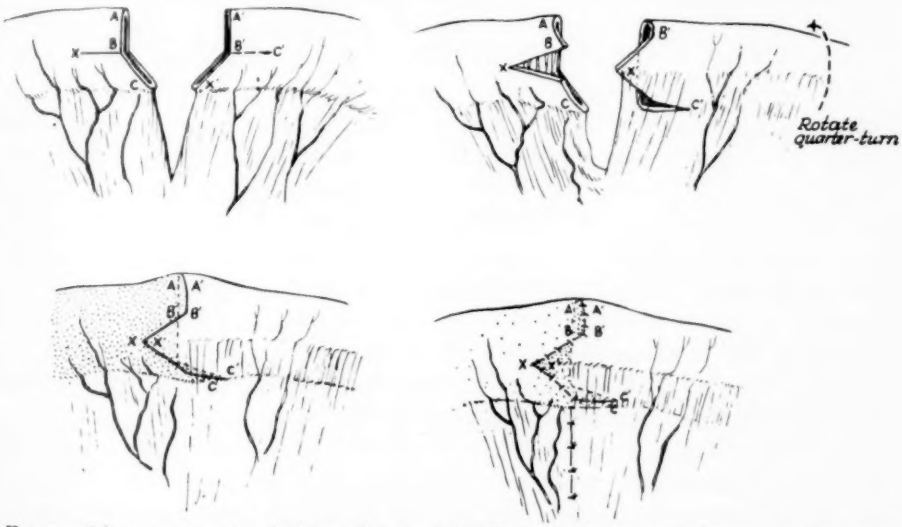

FIG. 4.—Diagram showing incisions for modified Z-plastic in an experimental hollow-tube anastomosed to prevent stricture.

and we have recently decided to investigate the practicability of applying plastic procedures to problems in visceral surgery. Clinical and experimental work in progress deals with methods of preventing postoperative constriction.

The amount of stricture which develops from a circular scar depends upon the size of the lumen of the tube as well as on the quantity of scar-tissue formation. In the large and small bowel, therefore, obstruction following ordinary surgical procedures is something of a rarity. In tubular anastomosis end-on in other parts of the body, however, strictures are frequent and troublesome, especially where a viscus is anastomosed to the skin, as in a short, single-barrel colostomy, a tracheotomy, after laryngeal resection, and in certain stages of operation for repair of hypospadias when the normal urethra is sutured to the

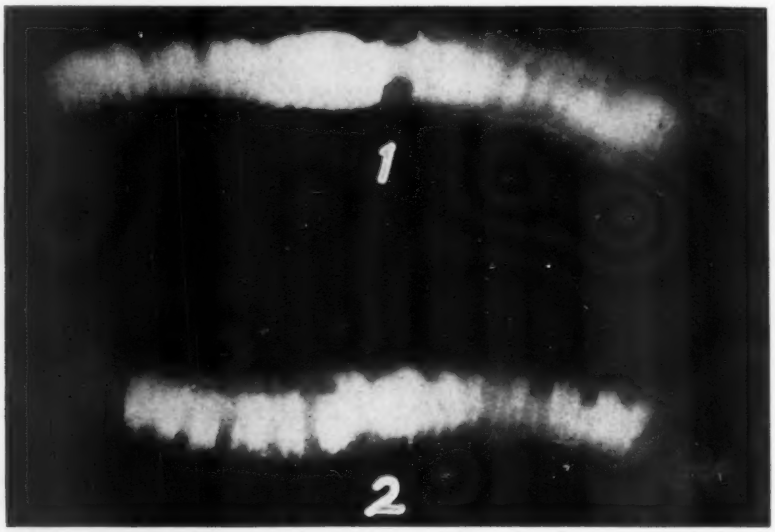

FIG. 5.—Roentgenogram five months after anastomosis in an experimental animal. (1) Conventional type. (2) Modified Z plastic.

artificial skin-formed tube. For the prevention of scar contracture in these instances, we advocate the use of a small triangular flap of skin to be sutured into a V-shaped opening in the margin of the hollow tube. So far we have had very good results in several patients with permanent tracheotomies (Fig. 2). This same method we employ in the repair of an external fistula of the parotid duct, which is dissected away from the cheek and brought into the mouth through a triangular incision.

The apex of the flap is sutured into a slit made on the side of the tube (Fig. 3). This procedure has also been reported by Thomas Stevenson. In the reconstruction of the esophagus by a skin-lined tube, the anastomosis to the stomach is accomplished with an inverted V-shaped incision to place a triangle of normal tissue across the line of tension and thus avoid a circular scar. At the present time, work is in progress, in collaboration with Dr. R. M. Moore and Dr. A. O. Singleton, Jr., to study postoperative results in experi-

mental animals following the use of similar triangular flaps in the common bile duct.

In addition to this preliminary investigation, we have been very much interested in devising a modified Z-plastic procedure to be employed in various types of tubular anastomosis to prevent stricture formation. In working out the method we have selected the small bowel of the dog as the most available material to observe for experimental purposes. In each animal a conventional end-on anastomosis was performed as a control, with the incision slightly oblique according to the usual practice. We next made in each animal a second resection and closure, employing a modified Z-plastic. In order to maintain abundant circulation, the triangular flaps which form the Z were placed in the mesenteric border of the gut. Incisions for resection were made as shown in

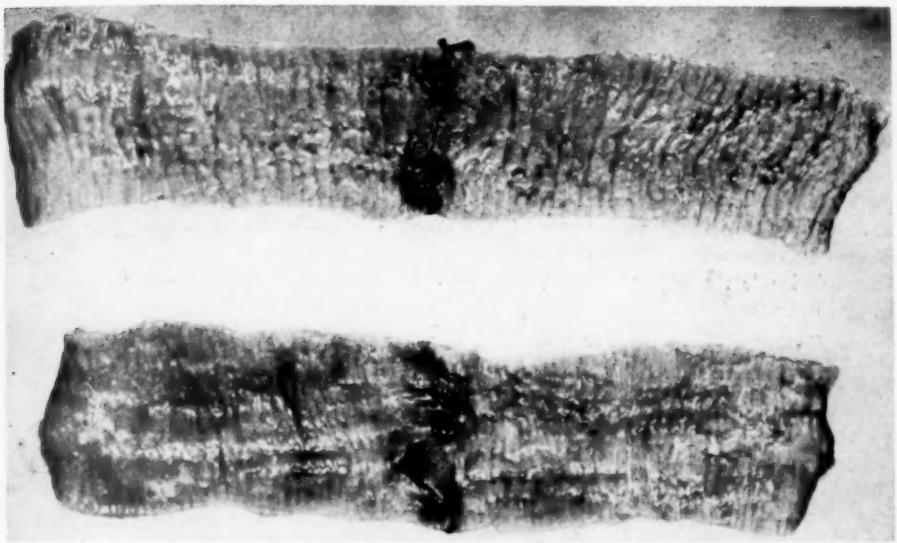

FIG. 6.—View five months after anastomosis in an experimental animal with the gut opened opposite the mesenteric border.

the diagram (Fig. 4). Perpendicular incisions were carried first midway through both sides of the bowel in each segment (AB and A′B′). They were then carried through the remainder of the bowel at an angle of 120 degrees down to the mesenteric border (BC and B′X′). A V-shaped portion of the mesentery was removed along with the resected bowel. Next a horizontal slit (BX) was made equal in length to the flap on the mesenteric border. A similar incision (B′C′) was made on the other surface of the opposite side. Now with a quarter-rotation of the bowel the two flaps thus made were transposed, bringing together points X and X′ and also C and C′. As may be noted, the mesentery now was present under each flap and the lumen of the bowel was considerably enlarged, as one would expect from the interposition of extra tissue. The procedures were carried out in eight animals, and after the lapse of

from three to five months there was still apparent, both by roentgen study (Fig. 5) and direct visualization (Fig. 6), an increase in the size of the lumen of the bowel in comparison with the site of the conventional anastomosis. We are hoping in the near future to employ the modified Z-plastic in smaller tubes where stricture often presents a genuine clinical problem.

CONCLUSION

Certain technics in surface operations which are considered to be within the province of reconstructive surgery are actually applicable to all branches of surgery and should be included in a comprehensive training program. The use of plastic principles in the solution of long-standing problems in general surgery is presented as a challenge which merits extensive laboratory and clinical experimentation.

DISCUSSION.—DR. E. A. KITLOWSKI, Baltimore: Unquestionably the use of Z-skin flaps in skin, rather than a linear incision, will offer better exposure and closure and will prevent many scar contractures which we have to contend with. In conjunction with the dressing Doctor Blocker mentioned in his excellent presentation, of necessity one must be a little careful that too much pressure is not exerted, for fear of interfering with the circulation of these flaps. Incidentally, in creating the flaps it is very important that the angles of the flaps be not made too sharp, so there will be no necrosis at the ends of the flaps themselves. I think if this method were applied as Doctor Blocker suggested to work inside the body, it would be a very important factor in the success or failure of the operation.

DR. ROBERT E. MORAN, Washington: I enjoyed this presentation very much. I am sure Doctor Blocker does not mean to infringe on the field of the general surgeon. I think he feels that there should be better co-operation between the plastic and the general surgeon. For example, in credentials for our Plastic Board, the plastic surgeon has to have one or two years of general surgical training. A general surgeon passing the Board seldom has the opportunity of any detailed training in plastic surgery. One important phase of plastic work is traumatic surgery as it comes into the general hospital. This is usually handled by the general surgeon; I speak now of automobile injuries in which there is a tremendous amount of damage to the face, etc. When one sees the case five or six days after the repair, the resident will say there was just too much bleeding to get good tissue closure, etc.

If you explain to the resident that the thing to do is to spread the wound wide and tie off the vessels, usually structures will be seen that we know go together. For example, in the old days we used to shave the eyebrows, but in severe injuries the eyebrow is an important landmark; the edge of the lid, the ala of the nose and the mucocutaneous junction of the lip are important. If we put together only tissues that we know belong together, we finish with a fairly good-looking face and there is little work for the plastic surgeon to do later. I have found that by talking to these residents and learning their problems, and having them come over on the plastic service for a few weeks, it has repaid splendidly by the fact that we seldom have to do much later with severe facial injuries.

DR. R. M. MOORE, Galveston: Doctor Blocker has described a method for the anastomosis of small tubes which seems to have several applications in surgery. I am not sure of its usefulness in dealing with the intestine. Probably there is no particular need for it in anastomosis of the adult intestine, which is of sufficient diameter that constriction

at the site of anastomosis is not a great problem. A method is needed to facilitate anastomosis of very small calibre intestine such as that distal to an atresia in infants. However, in this situation, the disparity in the size of the proximal and distal loops would make Doctor Blocker's technic scarcely applicable.

In end-to-end repair of divided or strictured common duct, on the contrary, the technic appears very useful. Dr. A. O. Singleton, Jr., and I have been doing some experimental work upon the common duct in dogs and have taken occasion to test this method of anastomosis. In dogs of average size the common duct is almost too small for accurate anastomosis unless it has been experimentally dilated by ligation of the distal duct a week or two previously. If such a dilated duct is sectioned and the cut ends are then anastomosed by this technic, the zone of anastomosis appears a widening in the duct rather than a narrowing, and still has this appearance some weeks later. This suggests that the method would be advantageous in repairing other small tubes such as the parotid duct and the ureter. It may also be useful in arterial anastomosis.

The method Doctor Blocker has shown for preventing contracture at a tracheotomy stoma can be applied to prevent skin contracture about a colostomy opening.

DR. T. G. BLOCKER, JR., Galveston: I certainly thank the discussers of the paper. I want to repeat again that I am not trying to demonstrate a method of anastomosing intestines. My primary objective is to show the value of this technic and its possibilities in anastomosing tubes that have their circulation in their entire wall.

THROMBOSIS AND EMBOLISM*

THE FIVE-YEAR EXPERIENCE OF A SMALL GENERAL HOSPITAL

ROY C. WIGGINTON, M.D. (By Invitation), WILLARD H. PARSONS, M.D.,
AND W. KENDRICK PURKS, M.D. (by Invitation)

FROM THE VICKSBURG HOSPITAL AND CLINIC, VICKSBURG, MISSISSIPPI

DURING THE FIVE-YEAR PERIOD ending January 1, 1948, phlebothrombosis, thrombophlebitis or embolism occurred after 40 of the 9,230 surgical procedures performed at the Vicksburg Hospital. The incidence of these postoperative vascular complications in this series of consecutive, unselected cases thus was 0.43 per cent. Twenty-one patients developed thrombophlebitis and eight developed phlebothrombosis, the initial lesion being followed by embolism in three cases in each of these groups. Eleven other patients developed embolism after operation in the absence of previously recognized phlebothrombosis or thrombophlebitis.

This is a relatively small series of cases, it is true, but it seems worth presenting for several reasons. It illustrates the universality of this particular problem. It emphasizes again the type of operation and the type of patients in which and in whom this type of postoperative complication is most likely to occur. It demonstrates the possibilities of prophylaxis and of therapy by a hospital staff which has become increasingly aware of the risks of postoperative vascular complications. Finally, and most important of all, it carries the lesson of errors which should not have been made and the losses which should not have occurred.

INCIDENCE

This series bears out, first of all, the paradoxical situation which is generally prevalent in respect to thrombosis and embolism. Over the period—perhaps 10 to 15 years—in which these postoperative complications have been recognized as susceptible to prevention and amenable to treatment, their incidence has increased notably.[1-5] In our own series there were five such complications in 1943 and the same number in 1944 against 16 in 1947, an increase out of proportion to the increase in surgical population of the hospital. The explanation, of course, for this as for a similar increase in most reported series, is that our recognition of these conditions has increased in proportion to our awareness of their possible development.

On the basis of the incidence reported in the literature, Barnes,[5] after making due allowance for the selectivity of reported cases, estimated that each year 34,000 persons in the United States die of pulmonary embolism. Whether or not one accepts these figures without reservation, there is no doubt of the potential seriousness of postoperative thrombosis and embolism. The incidence of these complications was low at the Vicksburg Hospital, as it usually is in a warm or semitropical climate. But there were seven deaths in the 40 cases,

* Read before the Southern Surgical Association, White Sulphur Springs, W. Va., December 8, 1948.

which is a high case fatality rate. Furthermore, these seven deaths were concentrated in the 17 cases of embolism, which makes the case fatality rate in that group appallingly high and makes clear once again that the best method of reducing the mortality of postoperative vascular complications is to endeavor to prevent the conditions from which emboli arise.

ETIOLOGIC FACTORS

Naturally the situation cannot be reduced to such simple terms. Not a great deal can be done about many of the predisposing and contributing factors beyond the exercise of special precautions in the cases in which these factors are known to exist. Our prophylaxis at the Vicksburg Hospital includes the use, after all operations, of exercises for the legs, deep breathing,

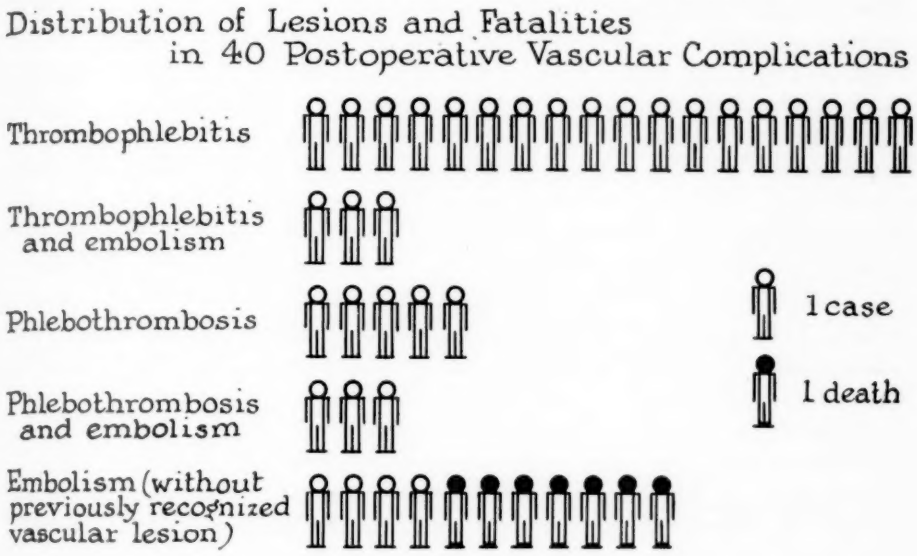

FIG. 1

frequent changes of position, sedulous avoidance of Fowler's position and early ambulation. In special cases the lower extremities are wrapped in elastic bandages from the toes to the groin. Digitalis is given to patients with cardiac disease, especially those with a history of cardiac failure. These precautions, however, do not prevent the bewildering fatal cases of pulmonary embolism, which exist in all series. The catastrophe comes to pass without any hint in the patient's previous history or clinical course that it is impending.

The data in this series are in general accord with those in other reported series. The majority of the patients (32) were women. Ten of the 40 patients were Negroes, who seem about as prone as white subjects to develop vascular complications after operation. It may or may not be significant that four of the seven fatalities occurred in this race, but there is no doubt that four deaths in 10 cases is an extremely high case fatality rate.

The statement that the age range in these 40 thrombo-embolic complications

was 21 to 77 is of no particular significance until the figures are broken down. Then certain facts become evident:

1. Of the 22 patients in this series under 40 years of age, four developed embolisms, one of which was fatal.

2. Of the 18 patients over 40 years of age, 13 developed embolisms, six of which were fatal.

3. Every one of the seven patients in the series who was 60 years of age or over developed an embolism, either abruptly or following clinically evident phlebothrombosis or thrombophlebitis, and five of the seven lost their lives as a result.

A series of 40 cases is far too small to permit statistically significant conclusions, but these figures cannot be discounted because they follow so closely the experience of others in respect to the age incidence and mortality of pulmonary embolism.

Our experience is also in line with the general experience that vascular complications are more likely to occur after certain types of operations and after certain conditions than after others. In this series, 13 of the 40 vascular complications occurred after hysterectomy and represented 3.8 per cent of all the hysterectomies performed during the five-year period surveyed. Ten occurred after other intra-abdominal pelvic operations and five occurred after plastic procedures on the perineum. In other words, 70 per cent (28) of the 40 cases of thrombosis and embolism in this series occurred after pelvic operations. Even more striking is the fact that three of the seven fatalities in the series occurred after hysterectomy, two of which were for carcinoma, while three other fatalities followed operations for carcinoma of the stomach and carcinoma of the breast. These figures again may be too small to be of statistical significance, but that does not detract from their clinical importance.

Six vascular complications occurred after 220 operations upon the biliary tract or resections of the stomach or large bowel, an incidence of 2.74 per cent. Although vascular complications are uncommon following surgery of the upper portion of the body, this series includes one instance of thrombophlebitis following thyroidectomy and one fatal embolism following radical mammectomy. One case followed incision, drainage and application of a cast for osteomyelitis of the femur and two occurred after open reduction of fractures of the lower extremity; in all three cases, one of which was fatal, immobilization was perhaps the principal etiologic factor. In only one other case in the series, to be mentioned shortly, was prolonged bed rest an apparent factor in the development of the vascular complication. The remaining cases in the series occurred after inguinal hernioplasty, closure of perforated peptic ulcers and application of a pedicle graft to a varicose ulcer. There were no postoperative vascular complications in the few splenectomies performed for hemolytic disease at the Vicksburg Hospital over the five-year period in question, which is interesting in view of Priestley and Barker's[6] contention that this operation is associated with etiologic factors likely to produce the highest recorded incidence of postoperative thrombosis and embolism.

Such predisposing causes as obesity, cardiac disease, blood dyscrasias, infection and extensive tissue resection, which are commonly accepted predisposing factors in the development of postoperative vascular complications, were all present, singly or in combination, in most of the cases in this series.

As has already been pointed out, in 11 of the 17 cases of pulmonary embolism in this series there was no evidence of a preceding thrombosis or thrombophlebitis, which suggests that in all 11 cases the emboli arose on a basis of silent, deep-seated phlebothrombosis. The fact that in no instance was a fatal embolism preceded by a clinically evident nonfatal episode can, we think, be accepted at its face value. The resident and visiting staffs in this institution are alert to the dangers of pulmonary embolism, and no time is lost in the prompt institution of anticoagulant or other therapy as soon as the presence of a postoperative vascular complication is recognized or suspected.

This series differs from certain reported series in that clinically evident thrombophlebitis was considerably more frequent (21 cases) than clinically evident phlebothrombosis (eight cases). We do not wish to emphasize this

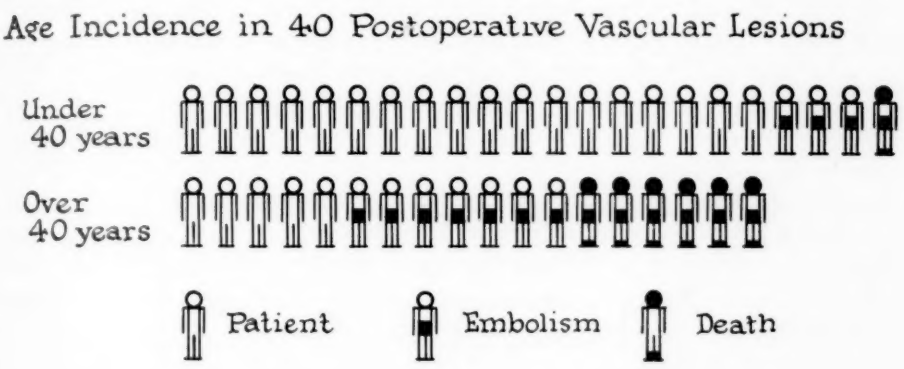

FIG. 2

disparity unduly, since it is apparent rather than real. In the remaining 11 cases, all of embolism, as has just been pointed out, phlebothrombosis was presumably present but was not clinically evident. On the other hand, it would be well to emphasize that pulmonary embolism may occur after the inflammatory vascular complication quite as well as after the so-called bland variety. Furthermore, as collected series prove, thrombophlebitis followed by embolism is fatal in perhaps 5 per cent of all cases.[7] It, therefore, seems wise to view it with considerably more concern than some authors now suggest it merits.

DIAGNOSIS

The postoperative vascular complications which make up this series were diagnosed chiefly on the clinical evidence, which was unmistakable in all cases. Roentgenograms of the chest were positive in only two of the five cases in which they were made, and electrocardiograms were positive in only two of four cases. The preponderance of negative findings is not surprising because,

with a single exception in each group, these examinations were made in non-fatal cases, none of which was very severe. The majority of patients with fatal embolism died too promptly—four of them within 10 to 35 minutes of the onset of symptoms—to permit diagnostic studies, even if they had been necessary.

Phlebography, as a method of diagnosing phlebothrombosis antecedent to embolism, was not employed in any case in this series. It has not been widely used, and one receives from the literature the impression that it is even less popular for this purpose at this time than it was when first introduced. How misleading this method of diagnosis can be is evident in the case mentioned by Linton,[8] in which a patient with normal bilateral phlebograms died 48 hours later from massive pulmonary embolism.

THERAPY

Since June 1, 1944, it has been the general policy at the Vicksburg Clinic to treat phlebothrombosis and thrombophlebitis with dicoumarol, whether or not other methods of therapy were used also. Exclusive of the seven fatal cases of embolism, in most of which death occurred too promptly to permit definite treatment, 26 of the 30 postoperative vascular complications which occurred after that date were treated with dicoumarol as the basic therapy. Three of the other four were treated by penicillin, venous ligation and paravertebral block, respectively. The fourth patient was removed to a Veterans Hospital shortly after an emergency operation for ruptured peptic ulcer and the details of the onset of the vascular lesion and of the therapy used are not known. Eight of the 26 patients treated with dicoumarol were also submitted to venous ligation and five were treated by paravertebral block; in one instance all three measures were employed.

In general, the plan of treatment was to administer 200 mg. of dicoumarol as soon as the diagnosis of phlebothrombosis or thrombophlebitis was made. Thereafter the prothrombin time of the blood was checked daily by the Quick method, and treatment was administered or withheld according to the results of this test. Twenty-seven seconds was regarded as the lower level of the effective therapeutic range and 60 seconds as the upper level of safety. The prothrombin time was kept within these limits by the administration of dicoumarol in appropriate dosages on any day on which a report of less than 40 seconds was received. These daily tests were made with the greatest care. Formerly, desiccated rabbit brain was used but recently desiccated rabbit lung has been found to be a more sensitive reagent. We have also begun to make the reports in terms of the percentage of normal activity rather than in seconds to avoid any possibility of misunderstanding on the part of the less experienced members of the resident staff.

If the prothrombin time was prolonged beyond 60 seconds, hykinone was given intravenously, in doses of 30 to 60 mg. The single instance in this series in which frank bleeding occurred was, by coincidence, the single instance in which dicoumarol was used prophylactically.

The patient, a 43-year-old white woman, had an episode of apparent thrombosis on the sixth day after vaginal hysterectomy, colporrhaphy and perineorrhaphy, 24 hours after prophylactic dicoumarol therapy had been begun. At the end of the sixth day of treatment, when the prothrombin time was 46 seconds, severe vaginal bleeding ensued. The drug was discontinued, hykinone was administered and a transfusion was given. Recovery thereafter was smooth, but 58 days later the patient re-entered the hospital with clearcut symptoms and signs, supported by roentgenologic evidence, of a pulmonary embolus, which cleared up under appropriate therapy.

It might be added that a nonfatal embolism occurred in a second case at the Vicksburg Hospital, not included in this series, 48 hours after dicoumarol therapy had been begun. The prothrombin time was only 23 seconds when the embolus became apparent.

With the exception of the hemorrhagic episode just related, patients in this series who were treated by dicoumarol recovered promptly from their vascular complications and indeed presented little cause for anxiety as soon as the prothrombin time had reached the desired therapeutic level. On the other hand, recovery was undoubtedly more rapid in the 12 cases in which anticoagulant therapy was supplemented by ligation of the femoral or saphenous vein, particularly when the clot was found and removed, and by paravertebral sympathetic block.

Thrombophlebitis was treated, in addition to the measures mentioned, by heat, elevation of the affected extremity and chemotherapy. Pulmonary embolism was treated by ½ gr. of papavarine and 1/100 gr. of atropine, both being given by the intravenous route. Oxygen was given by intranasal catheter, and other measures were employed as the special case demanded. We have not employed Evans'[9] recommendation that oxygen be combined with helium and given in the form of positive pressure respiration, nor have we had any experience with prolonged continuous spinal anesthesia as recommended by Smith and Rees.[10]

DISCUSSION

Although this series does not reflect the policy, we are coming more and more to believe that it is the part of wisdom to institute dicoumarol therapy on or about the fifth day after operation, regardless of the smoothness of their convalescence, in patients who present the factors likely to produce vascular complications. By this time the risk of bleeding as the result of anticoagulant therapy is reduced, while most vascular complications do not occur until this time or later. The onset of these complications is usually between the fourth and the twenty-first days.[2, 6, 11] In this series uncomplicated phlebothrombosis became evident between the fourth and fourteenth days after operation and uncomplicated thrombophlebitis between the fourteenth and twenty-second days. In 16 of the 17 cases of embolism the onset was between the fourth and fifteenth days; in 10 of these cases it was before the eleventh day. In the

remaining case, as already mentioned, it was on the sixty-fifth day after operation, following an attack of phlebothrombosis on the sixth day.

Anticoagulant therapy is particularly indicated in patients over 50 years of age—in whom, however, it must be used with caution, because of possible liver damage—in patients who are markedly obese, who have malignant disease, who have varicose veins or who have a previous history of phlebothrombosis or thrombophlebitis. We use it with great caution in patients with liver damage and we regard it as contraindicated after operations on the brain or spinal cord, in the presence of a blood dyscrasia or a bleeding tendency, in pregnancy near term and in patients who require a second surgical procedure within 14 days of the first. In all such cases, vein interruption is regarded as the indicated procedure. Venous ligation and division is also considered the procedure of choice in patients who have had a nonfatal embolism. Only time will tell whether those of us who, in general, prefer anticoagulant therapy to venous ligation as the basic therapy in postoperative vascular complications are correct, or whether experienced observers as Allen and his group,[12] Evans[9] and Zucker,[13] who prefer venous ligation for both prophylaxis and therapeusis, are correct in their position. Perhaps a combination of both measures will prove the answer to the problem.

Whether mass prophylaxis with anticoagulants would prevent postoperative vascular complications, or would even be justified, at the present moment seems highly debatable. In selected cases, in which difficulties are expected, the administration of dicoumarol is clearly indicated. But this form of therapy introduces a serious element of risk and if it were used routinely it might cause more deaths from hemorrhage than would be expected to occur if postoperative vascular complications were permitted to take their natural course. Moreover, it would add greatly to the burden of medical supervision, nursing and laboratory work, practical considerations which cannot be ignored in these days of shortages of physicians and nurses. The wiser plan for the present therefore seems to be to employ general prophylactic measures in all surgical cases and to limit anticoagulant prophylaxis to the special cases in which it seems indicated. DeBakey and Ochsner[14] also take the position that mass prophylaxis is not the solution of the problem.

For reasons of economy, we have not routinely employed heparin at the Vicksburg Hospital, but we believe that, in spite of this objection, it ought to be administered when indicated immediately after operation and continued until dicoumarol can be substituted and the prothrombin time has reached 35 seconds. The recently published experimental studies of Kiesewetter and Shumacker[15] on arterial trauma demonstrate that thrombosis is apt to occur promptly after trauma and that the most critical period from this standpoint is immediately after operation. Other studies by these same observers under controlled clinical conditions suggest that heparin combined with dicoumarol is even more effective than dicoumarol alone in the prevention of thrombosis after arterial injury and repair, and their observations seem entirely applicable to nonvascular surgery.

Embolectomy has never been attempted by us. The operation, while a theoretic possibility, is a practical impossibility. The circumstances which would make it effective simply cannot be met in practice, the chief difficulty being that if it is to have the slightest chance of success, it must be performed almost synchronously with the occurrence of the embolism. In the seven fatal cases in the Vicksburg Hospital series it would have been out of the question in four, in which death occurred between 10 and 35 minutes after the onset of symptoms, and almost impractical in a fifth, in which death occurred within three hours. The other patients lived 28 hours and seven days respectively, but neither was ever in condition to tolerate surgery of such magnitude.

This is the common experience. In a series of 78 fatal embolisms reported by Lam and Hooker[5] from the Henry Ford Hospital, half the patients were dead within 10 minutes of the catastrophe and 75 per cent within 30 minutes. Only 10 per cent lived longer than an hour. Even theoretically, therefore, not more than 25 per cent of these patients could have been benefited by operation. An additional practical consideration mentioned by the same authors is that more than half of the emboli in their series (56 per cent) became manifest between 5:00 P.M. and 9:00 A.M., hours when even a hospital prepared for quick emergency surgery is inevitably slower than usual in collecting equipment and personnel, particularly for an operation which is of such magnitude that it requires a surgeon of more than ordinary ability.

Since we practice early ambulation, it is ironic that one of the deaths in this series occurred in a case in which this measure could not be employed. A 65-year-old woman, somewhat anemic and with a cardiac difficulty, was submitted to radical mastectomy for malignant disease. This combination of predisposing causes strongly indicated early ambulation, but an attack of congestive glaucoma on the third day after operation made complete bed rest imperative. Death occurred on the ninth postoperative day, 35 minutes after the first symptoms of embolism became evident. In retrospect, this seems the type of case in which prophylactic dicoumarol therapy or venous ligation should have been instituted. The deceptive feature of the case was, of course, the fact that postoperative vascular complications are unusual after operations on the upper part of the body.

In this case, as in the six other fatal cases in our series, the simultaneous rise of temperature, pulse and respiration, emphasized by Allen and his associates[1] as indicative of impending pulmonary embolism, was not observed. There is no doubt of the value of this triad of symptoms and signs when it is present, but it is lacking in a large number of cases, just as it was lacking in our own series. Ochsner and DeBakey[14] noted that it was absent in 12 of the 25 fatal embolism cases which they collected from the New Orleans Charity Hospital. In eight of their cases there was antecedent clinical evidence of phlebothrombosis or pulmonary infarction or of both conditions. In five other cases there was a slight rise in the pulse rate, though the temperature and respiration were unchanged. In the other 12 cases there was no symptom or sign to suggest

the impending catastrophe, and that situation is, unfortunately, in line with the general experience.

SUMMARY AND CONCLUSIONS

1. The 40 cases of phlebothrombosis, thrombophlebitis and pulmonary embolism which occurred in 9,230 surgical procedures performed at the Vicksburg Hospital over a recent five-year period form a small series which is, however, typical in most respects of the clinical and other aspects of these complications. There were seven deaths in the series, all of which occurred after embolism, which came on catastrophically, without previous vascular episodes.

2. An analysis of these cases indicates the need for a careful application of general prophylactic measures after surgery and for the use of special measures in the cases in which predisposing factors exist.

3. Dicoumarol was used in 26 of the 30 cases in this series which occurred after June 1, 1944, exclusive of the seven fatal cases of embolism, in none of which anticoagulant therapy was employed. Experience suggests that recovery is prompter if venous ligation or sympathetic block is employed in combination with dicoumarol.

4. Prophylactic anticoagulant therapy, possibly a combination of heparin and dicoumarol, is probably indicated in selected cases, but mass prophylaxis by this means would introduce more problems than it would solve.

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DISCUSSION.—DR. ROY D. MCCLURE, Detroit: Through the years it seems that the deepest scars that have been left on most of us as surgeons have been the results of postoperative deaths that should not have happened. I felt in 1911, while working with Dr. Eugene Poole at the New York Hospital, that massage and early exercise in bed would reduce the number of thromboses and fatal embolisms. Then, while Doctor Halsted's resident at Johns Hopkins Hospital, I saw in five weeks on his service and that of Dr. Howard Kelly five deaths from embolism. We talked with Dr. J. J. Abel and Dr. William Howell about the possible use of hirudin but that proved to be too dangerous. When Doctor McLean, working on anticoagulants in Howell's laboratory, brought out heparin in 1916, we used it immediately after that in Detroit. The reactions, however, due to impurities, were so terrible in three cases that we never even reported it. It was not until about 1937 that the group in Toronto put out a purified heparin which was safe to use. We started using that in all cases which showed beginning pain in the calf of the leg. In spite of that we had in 1938 five deaths from embolism, four in 1940, five in 1941, three in 1942, five in 1943, eight in 1944 and 1945. However, that was in about 900 operations a month so it was not a large percentage, but we felt that these deaths should not have occurred. With the exception of two, not one of these fatal cases had specific treatment; the fatal cases came just as a bolt out of the blue.

The question is, how can we determine which patients will have thrombosis and pulmonary embolism. First of all, we agree absolutely with Doctor Parsons that age helps somewhat in predicting. In our series the occurrence is almost unknown under the age of 30. Certain types of operations, as he said, seem more prone to be followed by embolism. Gastrectomy, for example, led our list with 1.06 per cent deaths from fatal embolism, followed by colon and gallbladder operations and prostate operations, etc.

At the present time we have our residents watch very carefully the temperature chart and the calves of the patient's legs, during the postoperative period. An unexplained fever may lead to the giving of anticoagulants, on suspicion. The finding of a positive Homan's sign indicates to us immediately either a femoral ligation at the indicated site, or anticoagulant therapy, or possibly both. We give heparin immediately after operation. We used to give it preoperatively, but we had a few hemorrhages in the wound and gave that up. It takes about two days to get a positive effect from dicumarol. I speak knowingly because I myself have been taking it daily for ten months. What we have all hoped for was that someone would show us a test which would indicate to us an impending thrombosis and which would anticipate all the clinical signs just mentioned. Such a test was hopefully reported at the meeting of the American Surgical Association in Quebec last May by Mahoney and his associates.* Perhaps Doctor Morton can tell us of their subsequent experience.

They believe they have demonstrated the value of daily prothrombin times during the postoperative period, and if that time went down they would start anticoagulants. When I returned to Detroit from that meeting I was very enthusiastic about this and asked Doctor Barron and Doctor Lam of our staff to start this method immediately to see if we could anticipate which patients would have thrombosis and embolism. To date we have studied 179 cases. Each patient has eight prothrombin tests; one the day before operation, two the day of operation, and then one each day following operation for five consecutive days. Of the 179 cases, six have shown leg thrombosis without infarction, four have shown high prothrombin levels, but in two there was no elevated prothrombin as a warning. I feel sure our prothrombin estimations are well done. Seven patients had clinical phlebothrombosis of the lower extremity and also non-fatal pulmonary infarcts.

* Prothrombin Activity, Rachel S. Sandrock, M.D., and Earle B. Mahoney, M.D., Annals of Surgery, Sept. 1948, Vol. 128, No. 3.

In only two of these did the prothrombin curve give a warning; the other five showed perfectly straight prothrombin curves. One patient had a coronary occlusion during the study. His prothrombin curve gave no warning. As you know, the American Heart Association feels that in coronary thrombosis dicumarol has been a great aid in cutting down the number of deaths.

Of the patients who had had no clinical evidence of thrombosis, 64 had so-called elevation of prothrombin level and 98 were negative. We cannot say for certain that the 64 positives had no thrombosis, but they were not treated, and we have no reason to regret that we did not start anticoagulant therapy on them.

In summary, we have not been able to corroborate the findings of Mahoney and his associates that daily prothrombin determinations are of great value in predicting thrombotic complications, but further studies along this line are strongly indicated.

Dr. George T. McCutchen, Columbia, S. C.: I would like to recite an experience that lends emphasis to Doctor Parson's idea that it is well in some cases, particularly in those in whom you suspect embolism is likely to occur, to give some type of prophylactic medication. A little more than a year ago I encountered a patient who started with a primary disease in his chest. He was seen by his physician, X-ray films were taken, his clinical manifestations were similar to those of a small pulmonary embolus. He had pain in the chest and coughing of blood, but embolus was not suspected at the time. About two days later, on further questioning, it was found that he had had some soreness of his leg, in the calf, for three or four days prior to onset of symptoms.

On examination of the leg it was found that he had a positive Homan's sign, some swelling and tenseness of the calf. Ligation of the femoral vein was done and a clot was found at the point of ligation. During the next three or four months I encountered two other cases of a similar nature and was completely puzzled by the problem. I wrote to Dr. Mims Gage and Dr. Alton Ochsner, and they told me that so far as they knew this particular thing was unique; that they had never heard of it. Since that time there has been a total of seven patients with a similar syndrome; all in patients who had had no bed rest and in whom the leg had not been subject to trauma. We had to call in a term for it, and picked out one that rolled off the tongue very easily—spontaneous unprovoked phlebothrombosis. The last patient we saw might be questionable to some extent; a boy aged 15 who had had an appendectomy some five weeks before. He was ambulated immediately and had a completely uneventful convalescence. Nine weeks later, as he was entering an elevator, he was suddenly seized with pain in the chest and severe cough, and it was discovered that he had physical and X-ray indications of a pulmonary embolism, with pain, tenderness and swelling of the calf. That was the only one of the number who had, in recent weeks at least, been confined to bed.

It brings up an important point in diagnosis for our fellow internists as to some obscure conditions of the chest, and I wonder how often it might happen in cases of sudden death. None of these patients died; all had emboli of rather mild nature. We are completely at a loss as to the explanation of the cause of phlebothrombosis, I believe. Certainly we have to scratch our heads or stretch a point to believe that bed rest or trauma has much to do with it. So far as I am concerned it is still an imponderable problem, and one which is a long way from solution, and I believe it falls within the realm of the biochemist and the physiologist to produce the answer. I don't believe surgeons can. All these patients were subjected to elaborate study of the clotting mechanism and no abnormalities could be found. It remains for more delicate tests to be developed, or to find factors other than those we now understand as being causative in phlebothrombosis.

Dr. Frederic W. Bancroft, New York: Our experience with the tests for phlebothrombosis has been a good deal different from that of Doctor McClure. Doctor Stanley-Brown and I started this study in 1928, and at that time we made more than 4000 tests routinely on our surgical cases. It may be that the reason our results showed more was because at that time we did both prothrombin and fibrinogen tests, but in the series

we studied we had only one case, a breast amputation, done at another hospital, where there was no elevation of the clotting factors. The others had either high prothrombin or fibrinogen, and in the cases that developed accidents on routine study they had had warning signs before. So I do feel that we may find some method to ascertain which are the dangerous cases.

I was interested in Doctor Parsons' statement about the high percentage in hysterectomies. I think we have here possibly a different picture than in operations above the pelvis. I wish to report one case that illustrates what I mean. A woman had had a cesarean operation; a perfectly normal postoperative temperature; she had gone home, and on the tenth day afterward she had pain in the chest. She was brought back to the hospital and on X-ray it was a question as to whether it was an infarct or a virus pneumonia. Her legs were carefully measured; there was no tenderness and no swelling. However, seven days after onset of the pain in the chest, she had evidence of phlebothrombosis in the right thigh. I operated on her and took out the thrombus, but did not have a satisfactory suction apparatus, so did not feel that I had gotten entirely above the thrombosis. However, she apparently improved, but at the end of eight days after this she had pain in the chest again, and the X-ray showed an infarct in the opposite chest; seven days later she showed obvious thrombosis on the right. I operated on that side and she was given spinal anesthesia which I think was a mistake, because in flexing her forward I think they liberated another thrombus; anyway she died. It was obvious from the postmortem that the thrombosis had occurred primarily in the pelvic vein and had proceeded in a retrograde manner down her thigh.

A similar case is that of a woman who had had a normal delivery, and on the seventh postoperative day had pain in the chest, and X-ray evidence of pulmonary infarct —no evidence in the thigh. We went in simultaneously on both femoral veins; they were in spasm and did not contain a clot, but in passing a suction tube up to near the bifurcation of the vena cava we got clots from both sides and with anticoagulant therapy she went home five days later.

I think it is a difficult thing to know whether or not to use anticoagulants, or operation. I have done 35 thrombectomies, where the thrombus has extended above the femoral ligament. That one case is the only case of death; the rest have recovered satisfactorily. I have also given anticoagulants. I have not operated on any patient who had had a thrombosis for about ten days before being seen by me because I felt if they had thrown no embolus by that time, they were not going to, and that they could be treated by lumbar sympathetic block. I would like to say one word about our concept of early ambulation. Many of us have thought that if we got patients up and let them sit in a chair we were giving early ambulation. As a matter of fact that is the worst position we could possibly put them in for venostasis. The feet are much lower than they are in a Gatch bed, the knees are over the edge of the chair where there is compression on the popliteal veins, and there is sharp flexion of Poupart's ligament—all factors, I think, that aid venostasis. It is my idea that early ambulation is to get a patient out of bed, make him walk around the bed, get back into bed and lie flat, and not sit part of the time in a chair in as poor a position, probably, as we can get.

I wish to thank Doctor Parsons, and I enjoyed his paper very much.

Dr. Hugh A. Gamble, Greenville, Miss.: In the discussion of Doctor Parsons' paper there has been little said about the prophylaxis of postoperative phlebitis or thrombophlebitis. In 1934 I published in the American Journal of Surgery a description of what I called a bedcycle and later, in discussing a paper before this Association, described our method of preventing thrombophlebitis. Up to that time we were losing about one case out of every 1500 operations from pulmonary embolism. We had what seemed to be an epidemic of thrombophlebitis. A large proportion, at least one-third or one-fourth of the operative cases, would develop the condition and this began to be so much the case that patients in coming to the hospital would inquire as to what caused it and if there was any way to prevent it.

We went over the medical literature for the preceding 40 years. We found that Aschoff gave the most lucid description of the pathogenesis of this condition that we had seen. Adopting Aschoff's theory as to the causation of thrombophlebitis we had built what has been called a bedcycle. It is simply two bicycle pedals mounted upon a frame so that it can be placed upon the bed, and the patient is required to exercise his lower extremities on it for a period of five minutes twice a day, beginning the day of operation. While we felt that this was of extreme importance, we realized that during and following operation there is marked concentration of the blood, there is marked increase in the clotting elements present, and that it is at this time that the venous flow is at its lowest level. Therefore, we made it a practice of giving intravenous glucose in 5 per cent solution continuously through operations in an endeavor to maintain blood water levels. In order to promote the flow of venous blood we have routinely, for the first 24 hours following operation, required that these patients be given inhalations of carbon dioxide and oxygen every three hours for three minutes. Later on we began to get them up early, usually, where practicable, within the first 24 hours, requiring them to walk around the room. However, regardless of this we have maintained the use of the bedcycle throughout the whole period of hospitalization.

Since 1933 my brother and I have had something over 52,000 major operative cases. We have had one death from pulmonary embolism during this time. We have had seven cases of thrombophlebitis and I cannot but feel that these preventive measures have been effective in lowering the incidence of this condition.

The one death I speak of occurred in a man on the 21st day following operation. He had had a resection of the large bowel for carcinoma of the ascending colon and an end-to-side ileo-colostomy. He had had no symptoms suggestive of phlebitis of the lower extremities, but on that day he complained of pain in his lower abdomen and thought that he had eaten something that had disagreed with him. He was given an enema but was not entirely relieved of discomfort. At four o'clock in the morning of the 21st day I was called to see him and when I reached the hospital found him dead. An autopsy showed a large embolus in the right pulmonary artery, which had originated in the veins draining the transverse colon.

I feel that there is not enough attention paid to the fact that these embolic processes begin immediately after operation when the blood is at its highest concentration and the venous flow is at its lowest level and that, if you employ measures that will keep the water level of the blood up to normal and promote the flow of blood from the outset and keep it up from day to day, you will be convinced of the efficaciousness of this method of preventing these complications, which in some sections of the country seem to be so prevalent.

DR. ROY C. WIGGINTON, Vicksburg (closing): We would like to thank those who have so kindly and so generously discussed our paper. We, of course, do not believe that either anticoagulant therapy or vein interruption represent necessarily the final answer as to the therapy of venous thrombosis. We do believe, however, that perhaps careful evaluation of the risk in each surgical patient, determined by the criteria based upon the experiences of many who have studied the problem, will indicate those patients who should have dicoumarol as a prophylactic measure. We believe that the intelligent use of dicoumarol in this fashion might perhaps greatly reduce the mortality and morbidity incident to venous thrombosis, and might do so without posing impossible laboratory problems or unduly endangering lives.

At the Tulane University, and I believe at other places both in America and abroad, a great deal of work is now being done on the mechanism of blood clotting. At least two previously unknown factors have been discovered. As a result of this study many of the previous theories pertaining to blood coagulation may perhaps be discarded. It is further possible that those now investigating this phase of the subject may eventually solve the problem. Certainly, at the moment, its solution is by no means complete.

COMPARISON OF EFFECTIVENESS OF NEWER ANTIBIOTICS IN EXPERIMENTAL PERITONITIS: A PRELIMINARY REPORT*

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SINCE THE DISCOVERY of penicillin and streptomycin, other antibiotics are in the process of being studied and developed. Of the new group, chloromycetin and aureomycin are representative of types that should prove to be of value in certain surgical conditions.

Chloromycetin,† which is obtained from filtrates of submerged aerated cultures of a *Streptomyces sp.*, has been found to be quite effective against a number of rickettsiae, and several gram-negative bacteria. It was originally prepared by Ehrlich and associates from liquid cultures of a *Streptomyces* first isolated by Burkholder and shown by him to possess antibacterial activity. The crystalline substance is relatively insoluble in water, but well absorbed from the gastro-intestinal tract. It is well tolerated when given orally and serum levels of the drug after oral administration have been found to parallel those after parenteral injection. Its toxicity is apparently low.

In vitro, crystalline chloromycetin has been found to be inactive against yeasts and filamentous fungi, inactive against protozoa, moderately active against gram-positive bacteria and *Mycobacterium tuberculosis,* and active against gram-negative bacteria and *Borrelia recurrentis.* After single doses in the dog, only small amounts of antibacterial substances are excreted in the urine, indicating inactivation in the body and perhaps excretion by other routes.

Woodward[5] has demonstrated its clinical importance and significant chemotherapeutic effects in the treatment of typhoid fever. Pincoffs[6] recently reported its effectiveness in the treatment of Rocky Mountain spotted fever.

Aureomycin,‡ which is derived from a strain of *Streptomyces aureofaciens,* has been shown to possess, in vitro, antibacterial activity against numerous gram-positive and gram-negative bacteria.

It appears to be bacteriostatic, rather than bactericidal, except in high drug concentration. In experimental studies, no significant concentrations were obtained in blood serum more than 2.5 hours after the last injection was given, with a dosage rate of 20 mg. per Kg. of body weight, twice a day for ten days. Bryer[8] has reported that when aureomycin was administered orally to a 150-

* Read before the Southern Surgical Association, White Sulphur Springs, W. Va., December 8, 1948.

† The chloromycetin used in this study was supplied by Parke, Davis & Company.

‡ The aureomycin used in this study was supplied by the Lederle Laboratories Division, American Cyanamid Company.

pound (about 68 Kg.) man in doses of 500 mg. twice a day and 40 mg. intramuscularly every six hours, blood levels of 0.6 to 2.4 micrograms per milliliter of serum were observed one hour after an injection was given. The antibiotic produced a greenish-yellow discoloration of the urine, in which concentrations of 40 to 80 micrograms per milliliter were observed. He also reports that infections of the urinary tract due to coli aerogenes and *S. faecalis* have been sterilized and evidence of inflammation has disappeared when patients were treated with aureomycin by mouth.

It was thought that the properties of chloromycetin and aureomycin should render them valuable agents in the treatment of acute diffuse peritonitis due to mixed infections with both gram-positive and gram-negative bacteria.

Murphy *et al.*[1] have demonstrated that streptomycin hydrochloride injected intramuscularly will not only pass into the peritoneal cavity of normal dogs, but that the concentration of the drug in the peritoneal fluid may surpass the concentration in the blood.

Although there is a satisfactory test for the determination of chloromycetin levels, there is no comparable dependable test for evaluation of aureomycin levels. Aureomycin is quite unstable and additional study will be required in order to develop an accurate method of determining its levels in body fluids. In this study, no attempt was made to determine tissue fluid levels attained with the antibiotics studied.

The technic used to produce peritonitis in this study is one which was introduced by Bower and co-workers[3] and modified by Fauley and his associates.[4] Steinberg and Martin[10] have shown that a peritoneal infection diffuses throughout the peritoneal cavity fairly promptly after perforation of the bowel takes place. In their study of experimental peritonitis, they concluded that perforation of the gangrenous cecal wall was due to increased pressure, and could be produced by the instillation of air as successfully as when castor oil was used. A technic described by Silvani[12] for producing fulminating diffuse peritonitis was not considered applicable to this study.

TECHNIC

Animals were selected at random from stray, mongrel adult dogs, weighing from 15 to 20 pounds and excluding pregnant dogs, and dogs previously operated upon. The abdomen was shaved, scrubbed and painted with iodine and alcohol. Aseptic technic was rigidly observed. Under intravenous Nembutal Sodium anesthesia, the abdomen was entered through a right rectus incision and the appendix drawn into the wound. Mesenteric attachments were divided, and the appendiceal vessels were clamped, divided and ligated with silk. In order to minimize a tendency toward intussusception, the appendix was ligated 1 cm. from its base, with three coarse silk ties, rather than directly at its base (Fig. 1). The distal half of the appendix was then traumatized with a crushing clamp, the viscera replaced, and the incision closed in layers with silk. No drains were used and no dressings applied. Immediately after operation, each animal received 50.0 cc. of castor oil by stomach tube.

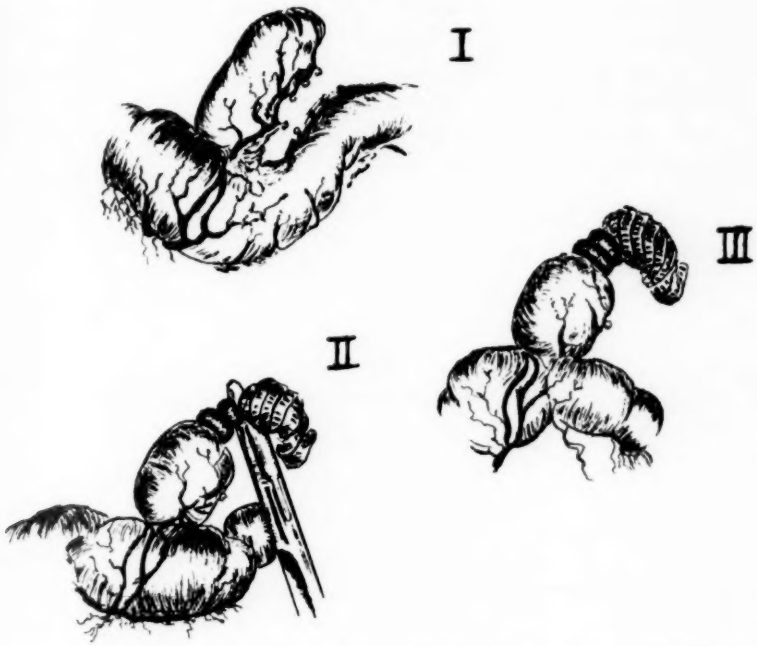

FIG. 1.—Technic for producing experimental peritonitis in dogs. (I) Dissection of stump and ligation of mesenteric attachments. (II) Crushing of distal end. (III) Ligation with three strands of heavy silk. Ligation for diagrammatic purposes is further away from the base than actually practiced.

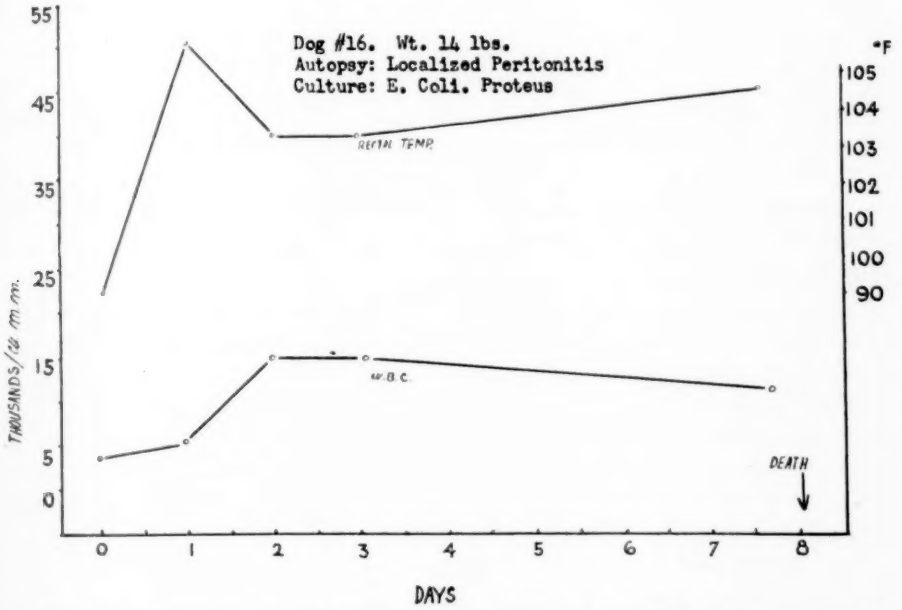

FIG. 2.—Typical course of control animal dying on the eighth postoperative day. Note sharp rise of temperature during the first 24 hours postoperatively. Minimum temperature (R) postoperatively, 103°F. with leukocytosis of 15,000.

No attempt was made to withhold food or water postoperatively, and no intravenous fluids were given. Temperature and leukocyte counts were determined every other day. Necropsy was performed on all fatalities shortly after death. All animals operated on are included in the series. The animals that survived were examined not earlier than 14 days after operation. Culture studies were made of peritoneal exudate in all animals.

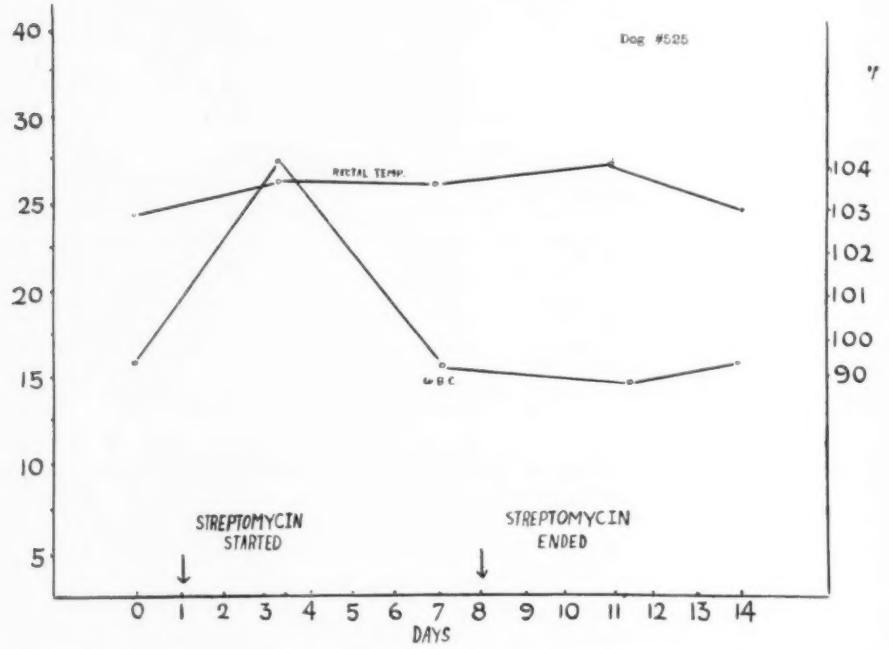

FIG. 3.—Typical postoperative course of dog treated with streptomycin. Maximum temperature (R) 104°F. with leukocytosis that became elevated to 28,000.

Although it is recognized that in peritonitis, penicillin probably enhances the effectiveness of streptomycin, and vice versa, it was not combined with any of the antibiotics studied.

Ten animals were used as controls. Of these, eight died of acute diffuse peritonitis, six of them within the first four days. Two animals recovered, a survival rate of 20 per cent (Fig. 2).

Ten animals were treated with streptomycin, starting 24 hours postoperatively and continuing for eight days. The dosage was 75 mg. every six hours intramuscularly, a dosage equivalent of 300 mg. every 24 hours. Of these, four died of peritonitis, three of them within the first six days. Six animals recovered, a survival rate of 60 per cent (Fig. 3).

Ten animals were treated with aureomycin, starting 24 hours postoperatively and continuing for eight days. The dosage was 100 mg. four times a day orally. Of these, only one animal died, this occurring as late as the ninth day. Nine animals recovered, a survival rate of 90 per cent (Fig. 4).

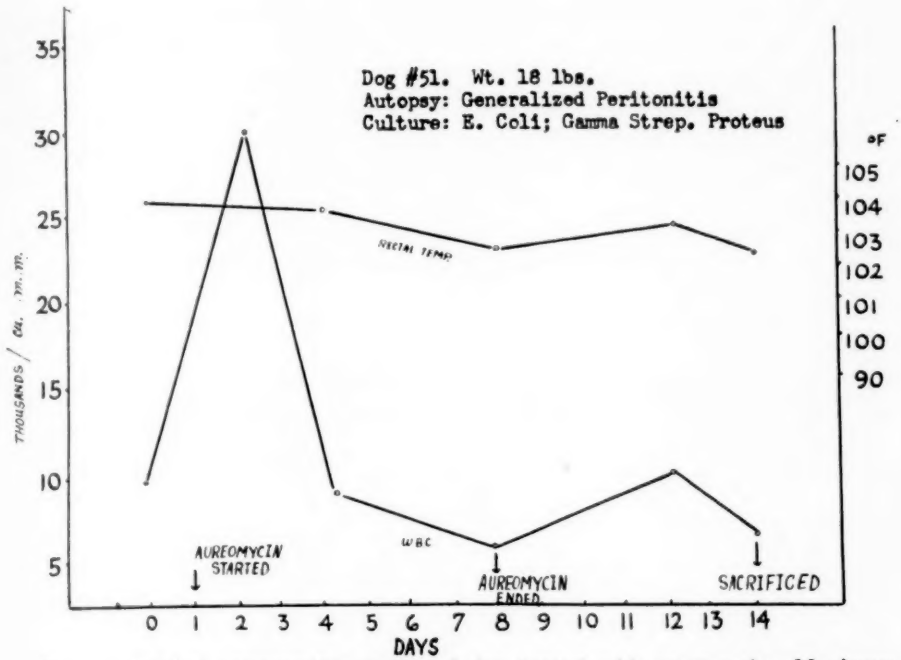

FIG. 4.—Typical postoperative course of dog treated with aureomycin. Maximum temperature (R) 103°F. with sharp rise of leukocytosis to 30,000 and dropping to within normal limits on the fourth postoperative day.

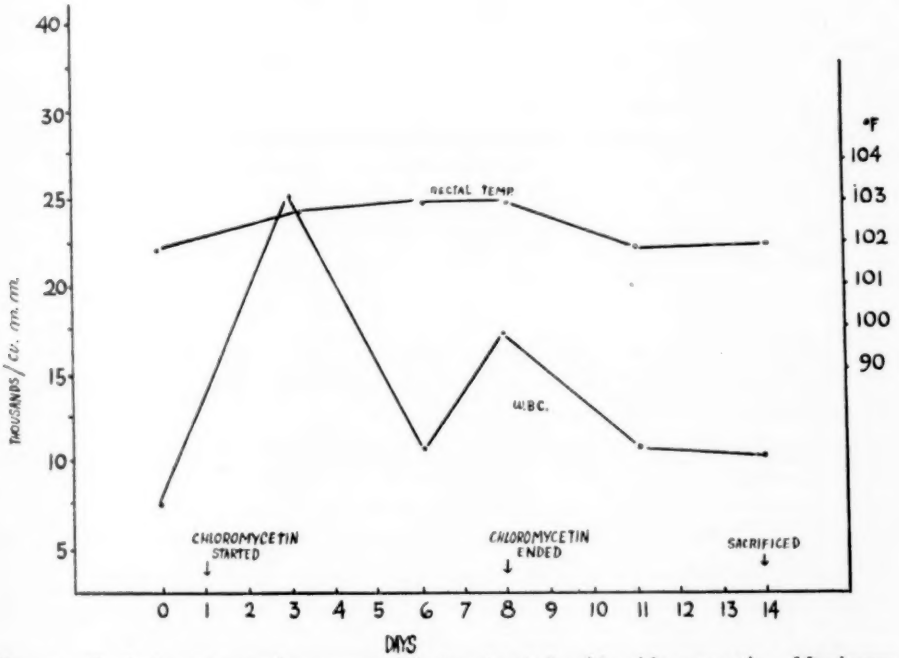

FIG. 5.—Typical postoperative course of dog treated with chloromycetin. Maximum temperature (R) was 103°F. with leukocytosis of 25,000.

Unfortunately, at the time of this study, chloromycetin was not available in sufficient quantity for a fair comparison with the above observations. However, the animals in which it was used survived with an initial oral dose of .25 Gm. followed by .062 Gm. every three hours. A larger series of animals are to be studied with chloromycetin therapy for more effective evaluation (Fig. 5).

All animals were autopsied as soon after death as possible, and peritoneal exudate culture studies made. In addition, all dogs that survived 14 days were sacrificed and culture studies made (Table I). Five control animals showed a predominance of *Escherichia coli*. Eight animals treated with streptomycin

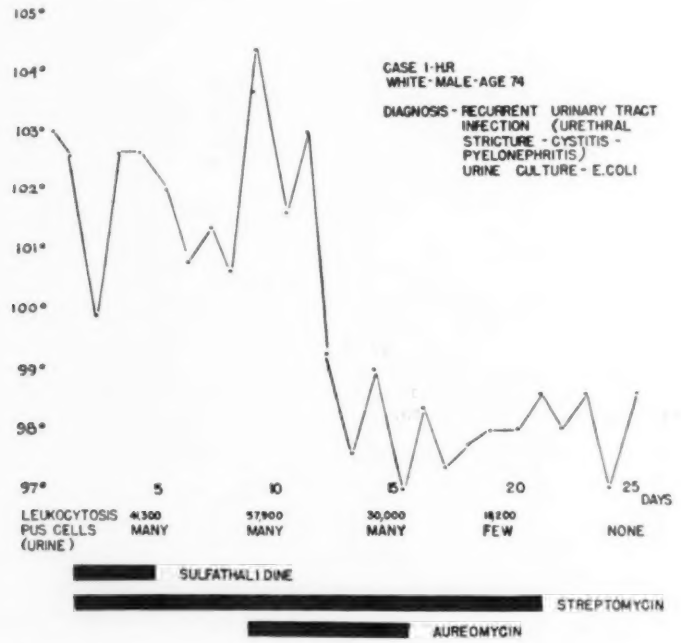

FIG. 6.—Clinical course of Case 1, H. R. Urinary tract infection with *Escherichia coli*. Following treatment with aureomycin, urine became culture free. Patient expired of a massive gastric hemorrhage after being ambulant and ready for discharge.

showed *Escherichia coli*, while only four treated with aureomycin showed this organism. It is interesting to note that of ten animals treated with aureomycin, eight showed various types of proteus organisms.

The comparative survival rates are shown in Table II.

CLINICAL STUDIES

Two patients with infections of the urinary tract due to *Escherichia coli* and two patients with a generalized peritonitis were treated with aureomycin with favorable responses.

Case 1.—H. R., No. 17022. White male, age 74, admitted to the University Hospital on September 15, 1948, with a complaint of pain in the legs and back associated with chills

and fever. Three months previously, he had been discharged from the hospital following a transurethral resection for benign prostatic hypertrophy. At the time of his previous admission, in addition to a benign prostatic hypertrophy, additional diagnoses of gastric ulcer, cystitis and pyelonephritis were made.

Admission specimen of catheterized urine, in addition to showing innumerable white blood cells, subsequently cultured *Escherichia coli* (Fig. 6). Temperature on admission was 103.2°F. He was immediately placed on 1 Gm. of sulfathalidine every six hours and 250,000 units of streptomycin every three hours. Sulfathalidine was discontinued after four days. Streptomycin was continued at the same dosage level. Urine cultures one week after admission continued to show *Escherichia coli* and *Pseudomonas pyocyanea*. His

TABLE I.—*Incidence of Bacteria Cultures from Peritoneal Exudate of Dogs with Experimental Peritonitis**

Organism	Controls (10 Dogs)	Streptomycin (10 Dogs)	Aureomycin (10 Dogs)	Chloromycetin (1 Dog)
Escherichia coli	5	8	4	1
Gamma streptococcus	4	5	3	0
Proteus	4	2	8	1
Clostridium perfringens	5	3	1	1
Staphylococcus albus	4	0	0	0
Streptococcus viridans	0	2	0	0
Beta hemolytic streptococcus	1	2	0	0
Staphylococcus aureus	2	0	0	0

* Note that *Escherichia coli* was cultured from eight of ten dogs treated with streptomycin, while eight of ten dogs treated with aureomycin cultured various proteus organisms.

course remained septic and extremely stormy. On September 23, 1948, or eight days after admission, his temperature rose to 104.4°F. He was placed on an oral dose of 1 Gm. of aureomycin every six hours for two days, following which the dosage was reduced to 0.5 Gm. every six hours. His temperature returned to normal in two days and he showed dramatic improvement.

Five days after starting aureomycin therapy, the urine became clear of white blood cells, and cultures were negative. After six days, aureomycin therapy was discontinued,

TABLE II.—*Comparison of the Survival Rate in the Treated and Untreated Animals**

	No. Dogs	Survived 2 Days	4 Days	8 Days	14 Days
Controls	10	8	6	4	2
Streptomycin	10	10	8	6	6
Aureomycin	10	10	10	10	9
Chloromycetin	1	1	1	1	1

* Note that 90 per cent of the dogs treated with aureomycin survived, and 60 per cent of the dogs treated with streptomycin. Only 20 per cent of the control dogs survived.

following which urine cultures again became positive. However, despite this, his leukocytosis decreased, and his temperature remained normal. He became asymptomatic and had been ambulant when he suddenly succumbed to a massive gastric hemorrhage. Subsequent autopsy revealed, in addition to a bilateral hydronephrosis, a benign gastric ulcer.

Case 2.—J. P., No. 26677. White male, age 72, admitted to the University Hospital with a diagnosis of recurrent carcinoma of the bladder. On August 16, 1948, a bilateral transplantation of the ureters into the sigmoid was performed. Postoperatively, he was placed on sulfathalidine 1 Gm. every four hours, and also 50,000 units of penicillin every four hours (Fig. 7).

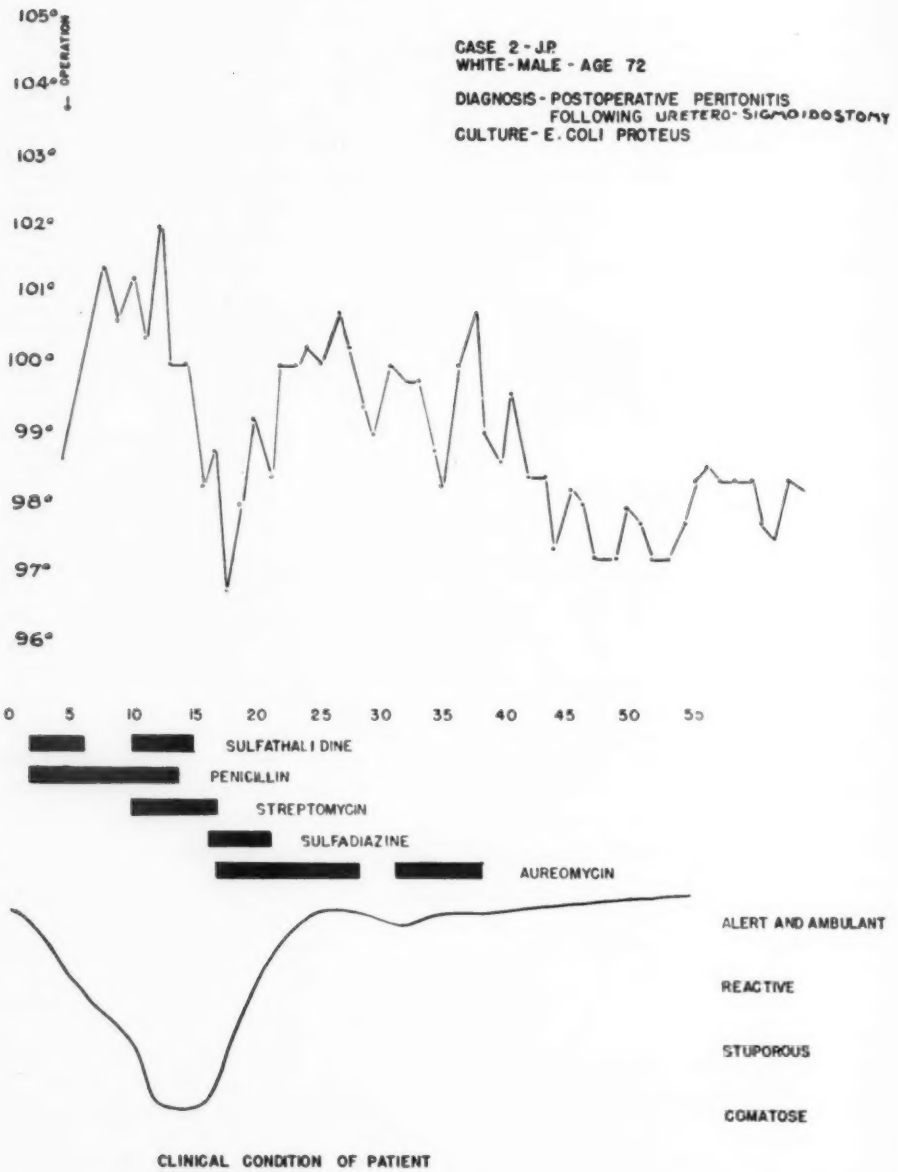

FIG. 7.—Clinical course of Case 2, J. P. Urinary tract infection with *Escherichia coli* and Proteus organisms. This patient was treated with sulfathalidine, penicillin, streptomycin and sulfadiazine in the order named. Aureomycin was started on his 15th postoperative day and two days before streptomycin was discontinued. Preceding the administration of aureomycin, he was comatose. Within 24 hours he showed marked response and within seven days after starting aureomycin, he was ambulant.

He developed evidence of a generalized peritonitis. A moderate dehiscence occurred and the incision drained copious quantities of foul smelling pus, which cultured *Escherichia coli.*

He was placed on 250,000 units of streptomycin every three hours, which was discontinued after one week when he failed to show improvement. Two days before discontinuing streptomycin, he was placed on 3 Gm. of sulfadiazine intravenously every day. After five days, sulfadiazine therapy was discontinued. When streptomycin was discontinued, he was placed on aureomycin 300 mg. intramuscularly every six hours. The dosage variation is shown in Figure 7. After sulfadiazine was discontinued, aureomycin was the only specific therapy given.

Preceding the administration of aureomycin, he had been comatose. Within 24 hours he showed marked response, and within 7 days his general condition had improved sufficiently to permit ambulation. Aureomycin therapy was discontinued after the twelfth day. Cultures of the abdominal wound at that time revealed a heavy growth of *Proteus vulgaris.*

Several days after discontinuing aureomycin, wound drainage increased and cultures showed a return of *Escherichia coli.* He was again placed on aureomycin. He improved immediately. He was discharged from the hospital on his 39th day, or 25 days after starting aureomycin therapy.

COMMENT. It is conceivable that when aureomycin was first discontinued and wound cultures showed a heavy growth of proteus organisms, chloromycetin might have been of value. In vitro, aureomycin is not effective against proteus organisms, while chloromycetin is quite effective.

The dramatic and speedy improvement upon the administration of aureomycin suggests a rapid control of toxins elaborated by the offending organisms, and recognized to be an important factor in the lethal effect of peritonitis.

Case 3.—H. O., No. 42236. Colored male, age 48, admitted to the University Hospital with a history of right lower abdominal pain, and vomiting of three days duration. A diagnosis of acute appendicitis with peritonitis was made. At operation, a gangrenous and perforated appendix was removed. The peritoneal cavity contained free, foul smelling turbid fluid, which, when cultured, yielded *Escherichia coli.*

Postoperatively, he was given 100,000 units of penicillin every two hours for two days, and afterwards 100,000 units every three hours. He was also given, intramuscularly, 40 mg. of aureomycin, in a buffer solution, every four hours. The dosage was varied as shown in Figure 8 until on the sixth postoperative day he was given 250 mg. of aureomycin orally every six hours.

His entire postoperative course was remarkably uneventful, and on the 15th day he was discharged from the hospital.

Case 4.—W. G., No. 18949. White male, age 39, admitted to the University Hospital with a history of pain in the right lower abdomen of one week's duration, not associated with nausea or vomiting. Admission temperature was 104°F. The abdomen showed a board-like rigidity. Diagnosis of generalized peritonitis was made. At operation, a gangrenous, perforated appendix was removed. Fecal material was found lying free in the peritoneal cavity. A generalized, loculated type of peritonitis was also found, with thick exudate. The pelvis was filled with pus. Fluid culture, which was foul smelling, yielded *Escherichia coli.* The abdominal cavity was drained.

Postoperatively, he was placed on 50,000 units of penicillin every three hours, and 500 mg. of aureomycin, orally, every four hours for five days. After five days, the same dosage level was continued every six hours instead of every four hours.

He was discharged from the hospital on his 14th postoperative day, asymptomatic and incision healed.

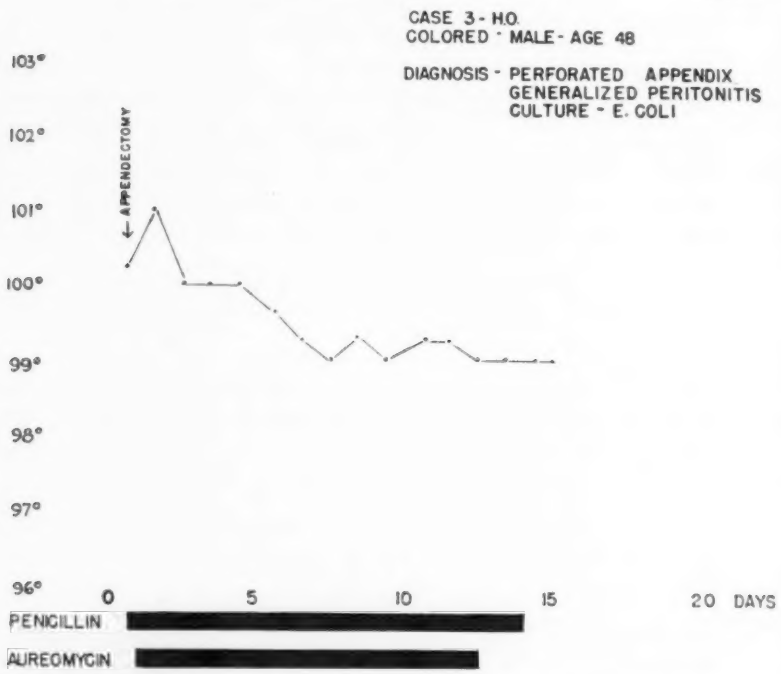

FIG. 8.—Clinical course of Case 3, H. O. with generalized peritonitis and cultured *Escherichia coli*. Patient treated with penicillin and aureomycin.

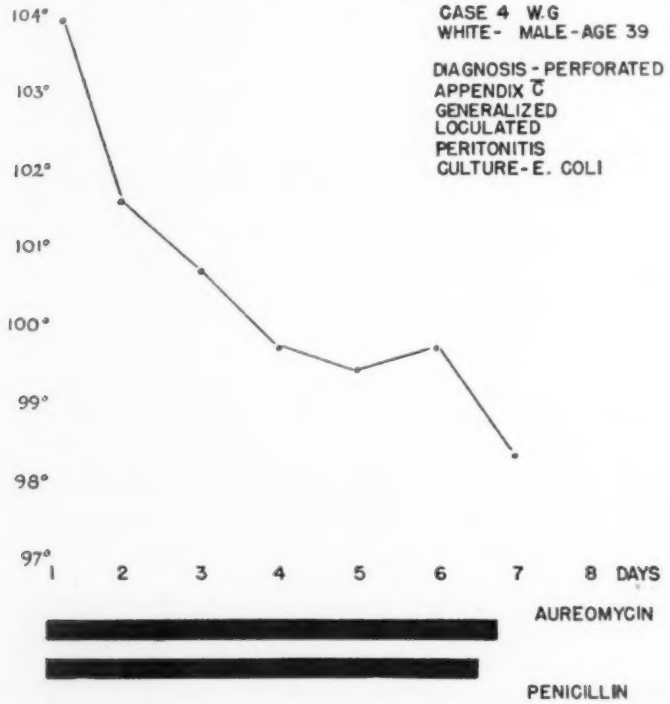

FIG. 9.—Clinical course of Case 4, W. G. with generalized peritonitis and cultured *Escherichia coli*. Patient treated with penicillin and aureomycin.

SUMMARY AND CONCLUSIONS

1. Experimental peritonitis has been produced in a series of dogs in an attempt to compare the protective significance of streptomycin and aureomycin.

2. The survival rate of the control animals was 20 per cent as compared with a survival rate of 60 per cent for those treated with streptomycin and 90 per cent for the dogs treated with aureomycin.

3. Chloromycetin shows suggestive evidence that it may have comparable value in peritonitis.

4. Two patients with *Escherichia coli* infection of the urinary tract and two patients with generalized peritonitis were treated with aureomycin with apparently favorable results.

5. Observations of other workers suggest that the major field of usefulness of aureomycin may be in the treatment of infections with rickettsia and certain of the virus group. The results noted in the present study warrant more extensive observations of its effects in a variety of bacterial infections.

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DISCUSSION.—DR. C. HAL INGRAM, Baltimore: I would like to say just a word concerning the technic that we used in producing peritonitis in experimental animals. Adult, mongrel dogs, weighing between 15 and 20 pounds, were used. All operations were done through a right rectus incision, observing aseptic technic.

The appendix was delivered into the wound, the meso-appendix was divided, and the blood supply to the appendix was carefully ligated with silk. The appendix was then triply ligated with coarse heavy silk about one centimeter from its base. After ligating the appendix it was crushed distally with an appendiceal crusher, hoping to cause necrosis. Following this the appendix was allowed to fall back into the peritoneal cavity and the abdominal wall was closed in layers with silk. No drains were inserted and no dressings were applied. Immediately postoperatively 50 cc. of castor oil was given by means of a stomach tube. No intravenous fluid was given and no effort was made to withhold food or water from the animal.

This chart represents the clinical course in the control animal. The temperature rapidly rose to more than 105 and was stabilized around 104. There was not a great deal of leukocytosis. Death occurred on the eighth day. Autopsy was performed and cultures were taken which were positive for *E. Coli and B. Proteus.* There were many loculated, localized abscesses throughout the peritoneal cavity.

This chart represents an animal treated with streptomycin. Twenty-four hours after operation he was given 300 mg. of streptomycin daily in divided doses. A leukocytosis occurred up until about the fourth day, which subsided by the seventh day. Treatment was ended on the eighth day. The animal was observed for another week and sacrificed on the 14th day. At autopsy this animal also had a generalized peritonitis with many loculated abscesses.

This chart represents an animal treated with aureomycin. Treatment was started within 24 hours. You will note the marked leukocytosis in the first 48 hours, that dropped rapidly in the next few days. Treatment was ended on the eighth day. The animal was observed for another week and sacrificed on the 14th day. At autopsy the animal was found to have generalized peritonitis. Positive cultures were for *E. coli* and *B. Proteus.* There was very little tendency to localization in this animal; however, he appeared very healthy and alert.

This is the record of one animal we treated with chloromycetin. Treatment was started 24 hours after operation; there was elevation of the leukocyte count with return to normal at the end of about six days. Treatment was ended on the eighth day and the animal was sacrificed on the 14th day. He also had generalized peritonitis.

This is a comparison of the survival rate in the animals that were treated. Only six of the ten controls survived the first four days; only two survived the entire two-week period. Sixty per cent of those treated with streptomycin lived two weeks and nine (90 per cent) of those treated with aureomycin survived for two weeks. The one treated with choloromycetin survived the 14-day period.

DR. CHARLES R. EDWARDS, Baltimore: When surgeons hunt for a new product with which to treat peritonitis it is a healthy sign. Through the years we have seen decreasing mortality from generalized peritonitis, but the mortality rate has not yet reached the point we desire. There is no doubt that a great many patients who have generalized peritonitis and now survive would have died a few years ago. But their survival cannot be credited to the use of the sulfa compounds and antibiotics alone. Good surgery, preoperative hydration and proper postoperative treatment contribute far more, in my opinion, than the antibiotics and sulfa compounds alone would contribute. I am not willing to agree with some men that you can safely close a peritoneal cavity where there is a general infection, and not employ drainage.

The morbidity of patients who have general peritonitis and who receive the gunshot preparations now available is probably greater than ever before; because in many cases of peritonitis that develop very obscure, hidden areas of infection or inflammation, or

both, recovery is prolonged. We still have a lot of gunshot wounds in civilians. Recently a 14-year-old boy went hunting and was climbing over a fence, holding the gun the wrong way, and the gun discharged and blew away most of his abdominal wall; also part of the stomach, all the transverse colon, part of the jejunum and part of the left ureter. The resident operated on him and restored most of these structures except that he had to use the two ends of the colon and bring them out as a double-barreled colostomy. With plenty of supportive treatment the boy survived the primary shock, only to run fever for a long time, and as the course progressed he began to flex his left thigh more and more and complained of pain in the region of the left hip. The operator removed a wad of felt from the shell from the left lateral gutter and the left iliac fossa. Intravenous pyelograms showed function of the left ureter to be satisfactory. Physical examination did not reveal a psoas abscess as would be anticipated because of the complaints, but later an extraperitoneal exploration revealed pulpy degeneration of the psoas muscle, which was responsible for all the symptoms. This had gone on for about five weeks.

Another case to illustrate this was in a man aged about 30, who was admitted 24 hours after a diverticulitis of the sigmoid colon had perforated; he had general peritonitis. He was operated on and drained and a colostomy was done, and he weathered the storm primarily only to run fever for a long time. He complained of soreness in the region of the right diaphragm, but it defied all attempts either by physical or x-ray examination to locate a subdiaphragmatic abscess, as was fully anticipated. After about six weeks of treatment he was permitted to go home and the day before I came down here he was readmitted. Tenting of the diaphragm was very definite, so he had harbored this inflammatory exudate, possibly infection, for about eight weeks. During the year we have had eight cases of generalized peritonitis that have behaved in this manner and, in my opinion, this indicates clearly that the sulfa compounds and the antibiotics that are now available are not sufficient to cure infection. They help to control it, but they do not eliminate it, and these cases will get into trouble later.

I think there is a possibility in these new compounds which will merit investigation, and the work will have to be proved clinically later.

THE EFFECTS OF INTRAMUSCULAR AND INTRATHECAL ADMINISTRATION OF STREPTOMYCIN IN NORMAL DOGS AND IN DOGS WITH MENINGITIS DUE TO *ESCHERICHIA COLI**†

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MENINGITIS DUE TO *Escherichia coli* is extremely rare in the adult under peacetime conditions (Rauch and Krinsky,[1] Thompson and Quinn[2]), although infection of the central nervous system by this organism occurs not infrequently in patients with penetrating wounds (Cairns,[3] Ecker[4]). On the other hand, this type of meningitis is frequently encountered in infants (Barrett, Rammelkamp and Worcester[5]). Indeed, Rauch and Krinsky,[1] after an extensive review of the literature, state that it is the most common type of meningitis in infants under three months of age. Before the use of chemotherapeutic agents which have been developed in recent years, the mortality rate of this disease was 80 per cent.[5]

The use of sulfonamides led to a number of reports of recovery in isolated cases,[2, 6, 7] but the development of streptomycin by Waksman and his associates[8] offers hope of an even more effective therapy of this and related forms of meningitis. Many of the gram-negative pathogenic organisms are highly susceptible to the antibiotic effects of streptomycin and most strains of *E. coli* are especially sensitive to the drug (Buggs, Bronstein, Hirshfeld and Pilling[9]).

It is well known, however, that in normal individuals intramuscular administration of streptomycin results in the appearance of only minute quantities in the cerebrospinal fluid (Anderson and Jewell,[10] Heilman, Heilman, Hinshaw, Nichols and Herrell,[11] Zintel, Flippin, Nichols, Wiley and Rhoads[12]). Although in the presence of meningitis, somewhat larger quantities of streptomycin reach the spinal fluid,[12, 13] it would naturally be anticipated that intrathecal administration of the drug would offer maximum effectiveness in the treatment of meningitis.

Anderson and Jewell[10] and Heilman *et al.*[11] observed no apparent irritative effects of intrathecal injection of streptomycin. Cairns, Duthrie, and Smith[14] reported a moderate pleocytosis after such injections in two patients with brain tumors. In one case of tuberculous meningitis and one case of meningitis due to *Ps. pyocyanea* (both extremely ill), the same authors reported "fatal reactions" immediately following lumbar subarachnoid injections of 100,000 units of streptomycin and they warned that "in acutely ill patients such injections are not free from danger!" Walker and Johnson[15] reported severe ataxia in

* Read before the Southern Surgical Association, White Sulphur Springs, W. Va., December 8, 1948.

† This study was aided by the Jack Fies Fund for Research in Neurosurgery and the John B. Howe Fund for Research in Neurosurgery. The streptomycin was furnished by Merck and Company at the request of Dr. Chester Keefer.

monkeys after cisternal injection of streptomycin and a cortical irritative pattern in the electroencephalogram after application of the drug to the cerebral cortex. Granulomatous lesions were produced by injection of streptomycin in the cerebral cortex.

On the other hand, Nussbaum, Goodman, Robinson and Ray[16] reported prompt recovery in three infants with influenzal meningitis treated with streptomycin intramuscularly and intrathecally.

Streptomycin therapy of meningitis due to *E. coli* has been reported in two cases (Shields,[17] Alexander[18]). Both patients (one an infant, the other an adult) had failed to respond to penicillin, both recovered after treatment, intrathecally and intramuscularly, with streptomycin.

Because of the existing uncertainty regarding the safety and efficacy of the intrathecal use of streptomycin, we have carried out studies and the effects of this agent in normal dogs and in dogs with meningitis due to *E. coli*.

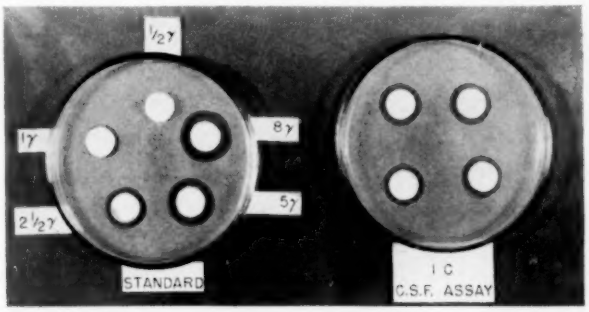

FIG. 1.—The "paper-disc" assay method for determination of streptomycin concentration.

METHODS

Streptomycin levels were determined by the "paper-disc" assay method of Loo, Skell, Thornberry, Ehrlich, McGuire, Savage and Sylvester.[19] The organism employed in the assays was Strain No. 103, G.M.S.-3 of *B. subtilis*. Assays were found to be extremely accurate and constant (Fig. 1).

The strains of *E. coli* employed for the production of meningitis were obtained from human infections, were tested for virulence and dosage in dogs and were kept in saline suspension in sealed ampoules in the frozen state, as described in a previous report.[20] Different "batches" of the cultures were employed in the three series of meningitis experiments (see below), but the organisms used in all animals in each series, both treated and untreated, were from the same "batch."

Dogs weighing seven to 12 kilograms were used in all experiments.

In four animals, intramuscular injections of 25,000 units of streptomycin were made at three-hour intervals and the level of the drug in the blood and cerebrospinal fluid determined in the same manner.

In each of six dogs, a single injection, ranging downward from 50,000 units to 5,000 units was made into the cisterna magna and the animal observed

for the effects upon temperature, pulse rate, respirations, clinical condition, and the cell count and streptomycin level in the cerebrospinal fluid.

In 100 animals *E. coli* meningitis was produced by injection into the cisterna magna of a suitable number of organisms suspended in 0.5 cc. of saline solution. Experiments were done in groups of ten. Five dogs of each group were treated, five untreated.

In a series of 40 dogs, treatment (in half the animals) consisted of daily intracisternal injection of 5,000 units of streptomycin, the first injection 30 minutes after the organisms were injected. Similarly, the treated animals in another group of 30 dogs received only intramuscular injections of 25,000 units

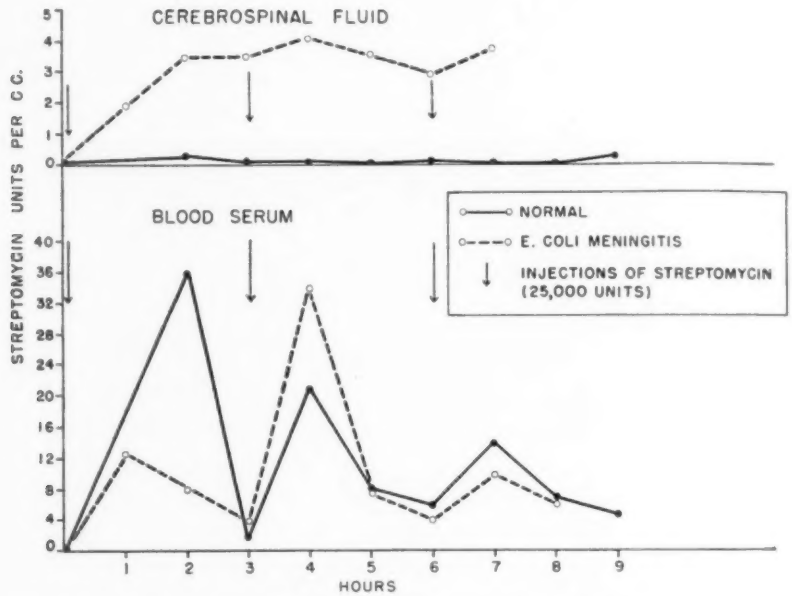

FIG. 2.—Blood and cerebrospinal fluid concentrations of streptomycin after intramuscular injection.

of streptomycin every eight hours, beginning immediately after the injection of organisms. In a third series of 30 dogs, the effects of combined intrathecal and intramuscular therapy were determined in the same way. Treatment was continued for seven days in all animals which survived that long.

Daily blood and spinal fluid cultures were made in all animals.

RESULTS

In normal dogs, intramuscular injection of streptomycin resulted in the appearance only of barely perceptible quantities in the cerebrospinal fluid. In dogs with *E. coli* meningitis, the spinal fluid concentration was distinctly higher, but a level of five units per cubic centimeter was the highest obtained. Typical examples of the two groups are shown in Figure 2.

Intrathecal injection of 50,000 units of streptomycin in a normal dog resulted in immediate stupor, profuse salivation, facial twitching and vomiting, followed by nystagmus and marked ataxia. Four hours after injection, the rectal temperature reached 106° F., respirations were 62 and shallow, pulse rate was 156. The spinal fluid white blood cell count reached 2190 at the same time and was 2700 24 hours later. Abnormal symptoms gradually disappeared within 48 hours.

TABLE I.—*The Spinal Fluid Cell Count and Drug Level After a Single Intrathecal Injection of Streptomycin*

		Time After Injection											
		1 Hour		2 Hours		4 Hours		6 Hours		24 Hours		48 Hours	
Dog No.	Dosage Units	Cell Count per cc.	Drug Level Units per cc.	Cell Count per cc.	Drug Level Units per cc.	Cell Count per cc.	Drug Level Units per cc.	Cell Count per cc.	Drug Level Units per cc.	Cell Count per cc.	Drug Level Units per cc.	Cell Count per cc.	Drug Level Units per cc.
SCS 1	50,000	210	1990	257	890	2190	262	1680	32	2700	23	675	9
SCS 2	25,000	30	1175	275	540	190	330	1000	150	220	19	75	9
SCS 3	15,000	72	588	220	376	7020	87	5100	32	272	11	110	4
SCS 4	10,000	32	640	100	440	*	80	*	14	1055	**	120	4
SCS 5	7,500	13	536	13	240	90	120	710	90	230	10	80	3
SCS 6	5,000	7	320	25	160	52	140	2250	67	182	9	52	3

* Blood in specimen.
** Unsatisfactory assay.

Following intrathecal doses of 25,000 units, 15,000 units, 10,000 units and 7500, the same symptoms and signs appeared with progressively diminishing severity and duration. With 5,000 units (roughly 500 units per Kg.) moderate lethargy and ataxia were the only symptoms and lasted only a few hours. A marked pleocytosis in the spinal fluid was found with all doses (Table I).

TABLE II.—*Survival Time, All Experiments*

	Treated	Untreated
Recovery	35	16
Less than 24 hours	11	17
24–48 hours	0	3
48–72 hours	0	4
3–7 days	3	5
Death after 7 days	1	5

All of these animals retained an effective level of the drug in the spinal fluid for 24 hours or longer (Table I). For this reason, 5,000 units was assumed to be the optimum daily dosage for dogs of this size.

The survival time in all animals with meningitis due to *E. coli* is shown in Figure 3 and Table II. Thirty-five (70 per cent) of the 50 dogs treated with streptomycin recovered as compared with 16 (32 per cent) of the 50 untreated dogs. Of the 15 treated dogs which failed to survive, eleven died within 24

hours, as did 17 untreated dogs. Excluding those animals who failed to live 24 hours, the recovery rate in the treated group was 89.7 per cent as compared with 48.5 per cent of the untreated group.

Differences in mortality rates in the three series of control animals are no doubt the result of use of three different preparations of the organisms. However, this does not affect comparative results in each series, since the same preparations were used in both treated and untreated animals of each group.

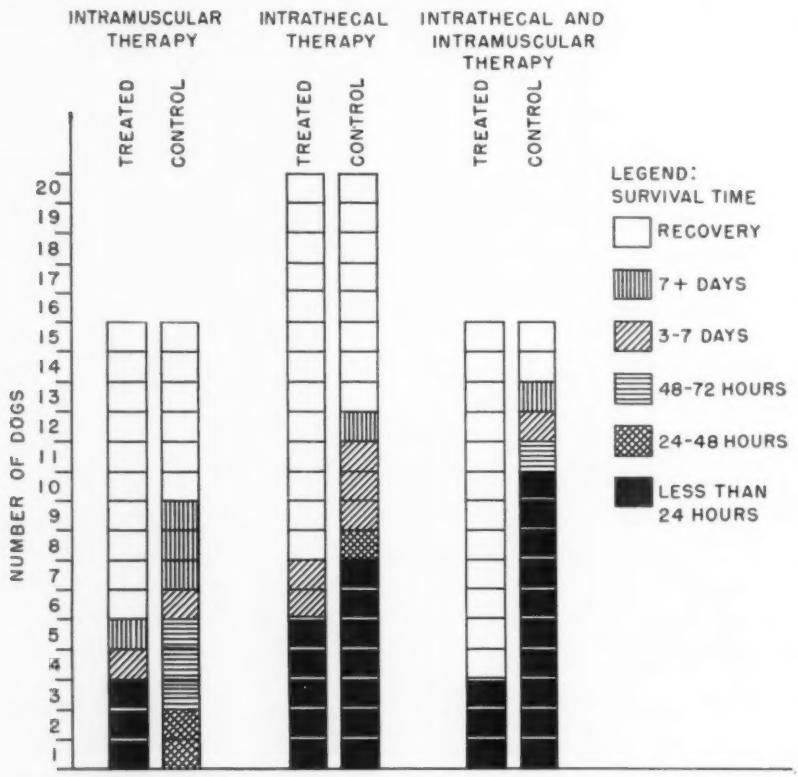

FIG. 3.—Survival time in meningitis due to *E. coli* in dogs; effects of streptomycin therapy.

Independent of this factor, there was a marked difference in the results in the three types of experiment (Fig. 3). Intramuscular therapy was limited in effectiveness. The recovery rate was greater in the treated group but the survival time in fatal experiments was greater in the untreated group.

The results of intrathecal therapy alone were more favorable as to both mortality and morbidity, but the differences were not great.

However, the combination of intrathecal and intramuscular therapy resulted in a highly favorable therapeutic effect in the treated animals (Fig. 3). Only two of 15 control dogs survived as compared with 12 of the 15 treated dogs. Evidently the preparation of *E. coli* used in this series was particularly virulent,

since 10 of the 15 untreated dogs died within 24 hours. This gives added significance to the high recovery rate in the treated animals.

Figures regarding duration of positive cultures of *E. coli* in blood and cerebrospinal fluid are difficult to analyze, since early fatality means short duration of positive cultures and higher mortality rate means fewer total days in which positive cultures could have been obtained. Despite this "weighting" of the statistics in favor of the untreated series, Table III shows an overwhelmingly unfavorable incidence of positive cultures in the untreated animals.

SUMMARY AND CONCLUSIONS

The effects of streptomycin have been observed in normal dogs and in dogs with meningitis due to *Escherichia coli*. Our observations seem to justify the following conclusions regarding the effects of this therapeutic agent in the dog:

TABLE III.—*The Duration of Positive Cultures in Blood and Cerebrospinal Fluid After the First 24 Hours*

Type of Therapy	Number of Days of Positive Cultures					
	Treated			Control		
	No. of Dogs	Blood	CSF	No. of Dogs*	Blood	CSF
Intramuscular	13	8	70	15	19	105
Intrathecal	15	1	25	14	10	102
Intrathecal and intramuscular	12	0	5	5	3	15
Totals	40	9	100	34	32	222

* Eliminating animals failing to survive 24 hours (see text).

1. In the normal dog, intramuscular injection of streptomycin does not result in the appearance of a significant amount of the drug in the cerebrospinal fluid.

2. In dogs with *E. coli* meningitis, intramuscular injection of streptomycin produces a slightly higher, but therapeutically inadequate level in the cerebrospinal fluid.

3. Intrathecal injection of large amounts of streptomycin may produce very marked irritative and toxic effects. The severity and duration of these effects is approximately proportional to the size of the dose.

4. The optimum daily intrathecal dose in the dog seems to be approximately 500 units of streptomycin per kilogram of body weight. This dose maintains an average 24-hour level of the drug in the cerebrospinal fluid approximately as high as do larger doses.

5. Intramuscular streptomycin in therapy of *E. coli* meningitis is ineffective.

6. Intrathecal streptomycin therapy of *E. coli* meningitis is helpful but inadequate.

7. Combined intrathecal and intramuscular therapy of *E. coli* meningitis

has a markedly beneficial effect upon mortality rate, survival time and duration of positive cultures in blood and cerebrospinal fluid.

Addendum: Since this work was completed, a paper by Lewin (Lewin, W.: Brit. J. Surg., **35**: 266, 1948) has reported eight cases of meningitis due to "coliform organisms" resulting from contamination of wounds. None of these was treated with streptomycin.

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DISCUSSION.—DR. WINCHELL MCK. CRAIG, Rochester, Minn.: The progress of medicine has been punctuated by new discoveries which have been used and tested for a final evaluation of their true worth. With the advent of the sulfa drugs and the other antibiotics much clinical and laboratory research has been necessary to determine the limitations of these drugs.

Foremost among those clinicians who have been conservative in the clinical uses of the antibiotics has been Dr. Cobb Pilcher. Again he has gone into the laboratory for the purpose of assessing the value of intrathecal and intramuscular administration of streptomycin in treatment of certain infections of the central nervous system. While *Escherichia coli* meningitis may be rare, the utilization of streptomycin in the combined method of administration follows the clinical application of the use of penicillin in treatment of other infections.

My colleague, Dr. Wallace E. Herrell who, as you know, has done a great deal of work with penicillin, tyrothricin and streptomycin, has commented upon the use of penicillin as follows: "Penicillin has proved exceedingly effective in the treatment of certain infections involving the central nervous system, including meningitis, wounds of the brain and brain abscesses. In the treatment of meningitis, penicillin should be administered by the intramuscular route and supplemented by 10,000 units of penicillin dissolved in 5 or 10 cc. of physiologic saline solution injected intrathecally every 24 or 48 hours for at least the first few days of the disease."

According to Herrell, many adverse comments upon the intrathecal use of penicillin and streptomycin are based upon the unfair evaluation following the use of too large amounts of the drug. Many authors who question the use of intrathecal administration do so because of the pleocytosis which sometimes occurs following its administration, and Pilcher's contribution to our knowledge of streptomycin helps clarify this point. Cultures of the spinal fluid should be made after 24 hours and at frequent intervals until a negative culture is obtained.

Pilcher has called attention to the fact that the concentration in the cerebrospinal fluid following intramuscular administration of streptomycin is greater than normal in infections of the central nervous system, because more of the drug can pass the blood brain barrier. And the therapeutic effectiveness of the drug administered intramuscularly is more effective when augmented by the additional intrathecal administration.

According to Herrell, intrathecal administration of this drug is indicated when high concentrations of streptomycin are desired in the cerebrospinal fluid. Single injections of as much as 100,000 units (100 mg.) in 5 or 10 cc. of isotonic solution of sodium chloride have been given intrathecally without evidence of serious reactions, and this amount may be given every 24 hours. Before the intrathecal injection is made, a sufficient amount of spinal fluid may be withdrawn to permit bacteriologic and other laboratory studies, including the determination of the level of streptomycin in the cerebrospinal fluid.

Streptomycin behaves not unlike penicillin when injected into the body. It diffuses rather readily throughout most body tissues and is excreted in certain body fluids such as urine, bile and milk. It differs from penicillin in the fact that even large amounts when given by mouth do not penetrate into the blood stream, making it an additional weapon in the preparation of patients for operation on the bowel. This is because streptomycin markedly inhibits the growth of the coliform organisms present in the fecal stream. Streptomycin is primarily effective against certain gram-negative microbes; whereas penicillin is effective against gram-positive pathogens.

Bacteriemia and infections of the urinary tract due to *Escherichia coli* have responded satisfactorily to streptomycin. There have been some failures in this group due to the fact that the organism was resistant or became resistant to streptomycin. Different types of meningitis have responded satisfactorily to treatment with streptomycin. These include infections due to *Hemophilis influenzae* and, in our series, we have one case of meningitis due to *Escherichia coli* which received streptomycin by both the intramuscular and intrathecal routes with a complete cure.

The toxic effects of streptomycin are somewhat similar to those of penicillin and respond in the same way following administration of one of the antihistamine drugs such as benadryl or pyribenzamine in doses of 50 mg. three times a day. In addition to the cutaneous toxic manifestations such as urticaria or irritative dermatitis, the toxic effects of streptomycin have been nausea, malaise, fever, renal irritation and arthralgia. These forms of toxicity are probably due to impurities. The dermatologic manifestations and involvement of the eighth cranial nerve were the ones most common. The latter results in tinnitus and dizziness and usually follows a long-continued administration of the drug.

Streptomycin can be given intramuscularly and intrathecally in combination with penicillin administered in the same way. In cases in which there is some question with regard to the effectiveness of a single drug, it has been demonstrated that sulfonamides and antiserums can also be employed safely.

As Doctor Pilcher has pointed out, meningitis from *Escherichia coli* is rare unassociated with penetrating wounds of the brain but, when meningitis does occur, caused either by *Escherichia coli* or other gram-negative bacilli, it is extremely gratifying to know that such studies as he has carried out make the intramuscular and intrathecal administration of streptomycin a safe procedure.*

Dr. Loyal Davis, Chicago: Doctor Pilcher and his associates have made another contribution to our knowledge concerning the methods, dangers and benefits of the use of the antibiotics in infections of the nervous system and its meninges. Their investigations upon penicillin and the sulfonamides were of basic importance, and to these they have now added important experimental data concerning streptomycin.

To avoid obtaining the wrong impression, it must be emphasized that in doses proper for his experimental animals, the benefits obtained from the intrathecal administration of streptomycin far outweigh its irritative effects. As a matter of fact, Ivy has shown that even the normal spinal fluid of a dog injected intracisternally, or intrathecally, into another dog, also produces irritative symptoms.

The circumstances are similar to those reported upon the effects of penicillin. When this drug was introduced into the ventricles and subarachnoid spaces of experimental animals, symptoms of marked irritation were produced. Yet we, with many others, have used penicillin in 100,000 unit dosages intraventricularly in children with meningitis without residual damage. We have also successfully followed the advice of Wycke of Australia, in using heparin to prevent the formation of a thick fibrinous exudate which often obstructs the cerebrospinal fluid pathways.

Doctor Pilcher points out again that streptomycin, to have its maximum effect, must be used intramuscularly and intrathecally, as is true of penicillin. Again, the effect of infection upon lowering the cerebrospinal fluid-blood barrier is demonstrated in their experiments.

Finally, I would ask only one suggestive question about these most excellent basic experiments. Would histologic study of the meninges and nerve tissue give any more assurance than is offered by evaluation of the clinical symptoms, that in proper dosage no permanent damage will result from the use of streptomycin in cases which are the clinical counterpart of Doctor Pilcher's experiments?

Dr. Cobb Pilcher, Nashville (closing): I want to thank Doctor Craig and Doctor Davis for their discussion. I do not think I can fully answer Doctor Davis' question regarding the histology and the effect produced by streptomycin in these experiments. I may say that sections of the middle ear, acoustic nerve and brain stem have not shown

* Herrell, Wallace E.: Streptomycin. Mississippi Valley Med. Jour. Oct. 1947. Reprinted by special permission from J. A. M. A., **132**: 200–205, Sept. 28, 1946.

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any significant effects of injury. We know that loss of hearing and loss of vestibular function are common in the use of streptomycin. My own feeling is that it is a dangerous drug, and it was with this in mind, as well as other points, that this study was undertaken. We have shown that large doses produce serious symptoms. We have also shown that small doses are safe in animals. The same general results have been found in clinical use, as well as with penicillin. We know that both drugs have a strong irritative effect in large doses intrathecally. Both drugs are still given in large doses, with complications which are usually attributed to the disease, rather than to the drug.

I think our paper should be taken as a warning against large doses of these drugs.

ULTRAVIOLET RADIATION AS AN ADJUNCT IN THE CONTROL OF POST-OPERATIVE NEUROSURGICAL INFECTION. II CLINICAL EXPERIENCE 1938–1948*†

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IN 1936, HART described the use of ultraviolet radiation for the reduction of postoperative infection from air-borne bacteria in the operating room.[1] In subsequent publications, Hart and his associates have presented in considerable detail the bacteriologic and clinical aspects of this problem in the field of general surgery. Only preliminary clinical studies were conducted among neurosurgical cases.[1k] This report will include our total experience with the use of ultraviolet radiation as an adjunct in the control of potential postoperative infection among 3,019 clean neurosurgical cases during the time period between January, 1938, and July, 1948. A preceding publication has described the effect of the exposure of atmospheric air plus ultraviolet radiation upon the brains of experimental animals.[2] No structural alterations were demonstrated in these studies that precluded the use of ultraviolet radiation upon the human brain nor has clinical experience suggested any untoward reaction in the exposed cortex when that structure is protected by the usual neurosurgical methods.

Although the complicated problem of postoperative infection has been examined at length by general surgeons, there is by comparison little direct experience recorded in our neurosurgical literature. Cairns, almost alone in his study of this field, has demonstrated without much doubt that neurosurgical postoperative infection does exist and represents a formidable obstacle to the attainment of consistently good technical results. The material of his first report[3] and a second review of later clinical investigations[4] may be summarized as follows:

	Operations	Infections	Deaths
1927–1938	968	?	23
May 1938–November 1944	1169	51 (4.4%)	13
December 1944–March 1947	670	6 (0.9%)	0

After November, 1944, Cairns began the prophylactic local use of a mixture of penicillin and sulphamezathine with an attendant marked reduction in

* See "The Effects of Ultraviolet Radiation on the Exposed Brain. Experimental Study," by Guy L. Odom, Henry M. Dratz and F. V. Kristoff, to be published in the July ANNALS OF SURGERY.

† Read before the Southern Surgical Association, White Sulphur Springs, W. V., December 8, 1948.

infection rate. He states that the six infections recognized during this period were severe and might have been fatal without vigorous antibiotic therapy.

A subsidiary but important by-product of this effort in the reduction of postoperative infection was the finding that the brain may be susceptible to infection by organisms normally regarded as saprophytes or contaminants.[5]

A second as yet unpublished summary of the incidence of postoperative neurosurgical infection has been made available to us through the generous co-operation of Dr. Wilder Penfield, Director of the Montreal Neurological Institute.[6] Every possible effort has been made in that clinic to control the many factors perhaps responsible for postoperative infection. Doctor Penfield's results are particularly significant since they illustrate a reduction in infection rate through the adjuvant use of a modified form of ultraviolet radiation. A definition of the character of these infections is not available. The yearly infection rates are given by Doctor Penfield as follows:

Year	Cases	Number of Infections
1942–43	695	4
1943–44	760	10
1944–45	858	11
1945–46*	968	4
1946–47	871	2
1947–48	914	4

* Installation of modified form of ultraviolet radiation.

The recognition by Cairns and Penfield of the existence and danger of postoperative infection among neurosurgical cases has in each instance resulted in the steady reduction of the infection rate, by different methods, to a relatively negligible factor. If further evidence is required to substantiate the fact that the problem of neurosurgical infection is a real one, and often unanswered, it may be obtained by reading the neurosurgical literature of the time period covered by our report. In four American surgical and neurosurgical journals in the time period January 1, 1938, through January 1, 1948, 2,710 clean neurosurgical cases are reported, among whom 20 patients died as a sequel of postoperative infection.

The statistical data of our survey, with a brief discussion of the findings, are as follows

TABLE I.—*General Summary*

Total clean operative procedures			3,019
Total infections			42
Severe	12	.4%	
Mild	25		
Stitch abscess	5		
Deaths attributable to infection			1
Infection percentage rate			1.39

TABLE II.—*Infections per Year*

	Number of Procedures	Infections	Deaths
1938	170	0	0
1939	202	2	0
1940	275	3	0
1941	190	4	1
1942	232	0	0
1943	210	2	0
1944	252	4	0
1945	321	5	0
1946	425	11	0
1947	477	9	0
1948 (6 months)	265	2	0
Totals	3,019	42	1

TABLE III.—*Infections in Specific Operative Procedures*

	Number of Cases	Number of Infections		Deaths
Craniotomy	1,228	13	1.05%	1
Removal of ruptured disk	1,063	19	1.77%	0
Laminectomy	271	6	2.21%	0
Other*	457	4	.90%	0

* Includes procedures such as lobotomy, trephine removal of extradural or subdural hematomas, resection of meningoceles, peripheral nerve operations, sympathectomies, scalenotomies, ligation of internal carotid artery in the neck, and the like.

TABLE IV.—*Predominating or Single Infecting Organism*

Hemolytic *Staphylococcus aureus*	14
Nonhemolytic *Staphylococcus aureus*	10
Nonhemolytic *Staphylococcus albus*	5
Culture negative	13

DISCUSSION

The duration of hospitalization or the duration of secondary wound healing, the intensity and length of elevated temperature rates, the threat to life or bodily function and the necessity for intensive antibiotic therapy were factors by which the severity of any one infection in this series was measured. Twelve infections were considered to be severe, 25 mild and five were noted as simple stitch abscesses. The incidence of infection was higher in lumbar laminectomies than in craniotomies or upper spine laminectomies. The rate of the severe infections was approximately .4 per cent.

In seeking a cause for individual infection, other than the acknowledged one of air contamination, it is interesting that 27 of the infections were related, if not directly attributable to defects in neurosurgical technique or errors in neurosurgical management. Thus, 12 infections followed the early appearance of operative hematomas, either with or without wound disruption,

five were subsequent to scalp flap necrosis, two appeared when craniotomies were drained through an adjacent stab-wound, two were related to the retention of foreign bodies (triangular fluffs), two occurred in disc procedures in patients who harbored a single cutaneous furuncle, one in a patient with a mild generalized dermatitis, one followed repeated ventricular taps, one occurred in a craniotomy wound that had been packed to control hemorrhage, and one was noted ten days after a tantalum cranioplasty of exceptional magnitude. If these infections were related to extraneous factors, the number presumably due to contamination by air-borne bacteria is significantly reduced.

Among the infections in which a positive culture was obtained, the organism represented some type of staphylococcus, a finding that has been previously demonstrated by Doctor Hart. No seasonal variation was noted in the relatively few infections. The average hospital stay for the patients with any form of infection, severe or mild, was 29.4 days as compared to the average stay for all patients in the year 1947 of 12.7 days. These patients were operated upon by two staff neurosurgeons and the resident neurosurgeons present during the ten-year period of the study.

Summary of case fatality attributed to infection:

Duke Hospital History A-52261, colored male, age 17, was admitted in a stuporous condition to the Neurological Division of the Medical Service on December 3, 1940. Generalized headache had developed 4 weeks prior to admission and the patient had become comatose 4 days before admission. Neurological examination showed, in brief, bilateral papilledema, right hemiparesis and hyperreflexia of the right-sided muscle-tendon reflexes. A provisional diagnosis of tuberculous meningitis was entertained and lumbar puncture demonstrated 100 mononuclear cells, a positive Pandy reaction and increased subarachnoid pressure. All other studies were essentially normal. A left frontal craniotomy was subsequently performed (B. W.) and the left frontal lobe was resected. The resection plane passed through a necrotic neoplasm situated in the base and lateral border of the anterior horn of the ventricle and extending caudally in the temporal lobe. On the seventh postoperative day, in spite of repeated ventricular drainage to reduce pressure, the medial limb of the craniotomy incision ruptured. Later culture from the persistent cerebrospinal fistula showed the presence of non-hemolytic staphylococcus aureus. Death occurred 22 days after operation and autopsy revealed a purulent leptomeningitis. The tumor, disclosed at operation, invaded the left fronto-temporal region, crossed through the corpus callosum and infiltrated the right frontal lobe. The pathologic diagnosis was glioblastoma multiforme.

SUMMARY

Ultraviolet radiation has been used as an adjunct in the prevention of neurosurgical infection during the time period between January, 1938, and July, 1948. Clinical experience with 3,019 clean neurosurgical cases has demonstrated subsequent wound infection in 42 of these cases, an incidence of 1.39 per cent. Twelve of these infections were severe, 25 were considered mild

and five were recorded as simple stitch abscesses. Staphylococcus aureus and albus were the predominating infecting organisms. A considerable number of wound infections appeared to be related, not only to the factor of bacterial contamination from the air, but also to errors in neurosurgical technique and management. In our opinion, this clinical study over a ten-year period indicates that ultraviolet radiation should be considered an important adjunct of the neurosurgeon's armamentarium.

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Discussion.—Dr. Deryl Hart, Durham, N. C.: I believe Doctor Woodhall has leaned backward in including every possible infection in his cases, and in ascribing the one death to an operating room infection; that is, an infection originating during the operation. This man disrupted his wound ten days after operation and died 22 days following operation, at which time there was infection in the wound after it had been draining for 12 days.

In the publications I have made on unexplained infections in operative wounds, we eliminated all the cases where there was an evident cause of infection, such as operation

on a perforated appendix, prolonged drainage of a wound, such as Doctor Woodhall reports, *etc.*

Before we introduced ultraviolet radiation in the operating room we had a number of severe, unexplained infections. Infections occur in cycles associated with bacterial spread over the country. Everyone is familiar with the spread of streptococcal organisms following the 1918 epidemic of influenza and the prevalence of streptococcal wound infections which followed. In the course of six years, during which we had 15,000 operations in a new hospital, we had 17 unexplained deaths in clean wounds. These were serious infections with meningitis, septicemia, and peritonitis predominating; all were fairly large operative procedures, mostly thoracoplasties, orthopedic operations or cranial operations. We did not have fatal infections in the general run of operative procedures, but occasional infections did occur.

The organisms in fatal and non-fatal infections were predominately Staphylococci. As illustrating the cyclic curve of infections, I would like to call attention to the fact that in one three-month period we had 35 per cent of all deaths from "unexplained" infections in this five-year period while we were doing approximately 1.5 per cent of the total number of operations. At this time in December, January and February, there was an epidemic of *Staphylococcus aureus* contamination of the nose and throat in the people of the community; 75 per cent of the people in the operating room personnel and in the general population had this organism in their noses and throats. During such time infections are almost inevitable if many large surgical operations are performed without some provision for preventing organisms from entering the air or for killing them in the air. The number of organisms in the air of the operating room diminishes greatly during the summer. When the organisms are in the noses and throats in great number, they are also in the air.

Doctor Woodhall and other members of the staff started using ultraviolet radiation at their own request, and it is now used routinely for most large clean operations. Between 50,000 and 100,000 operations have been performed in the Duke Hospital during the past 10 years. About 10 per cent of these have been large, clean procedures protected with ultraviolet radiation.

I have not made a complete survey recently, but have followed the matter of infections closely and I do not believe that there has been any death resulting from an unexplained infection during this period, unless this one reported by Doctor Woodhall is considered as unexplained.

REDUPLICATION OF THE STOMACH*

REPORT OF A CASE

GEORGE T. MCCUTCHEN, M.D.

COLUMBIA, S. C.

REPRODUCTIONS of the gastro-intestinal tract are a relatively uncommon occurrence. The term "enterogenous cyst" has been applied to these reduplications, which may occur in any part of the gastro-intestinal tract from the esophagus to the sigmoid. They are most commonly seen in the ileocecal region and decrease in frequency generally proximal to this point. About 15 cases have been reported in the literature as occurring in the duodenum, and the case reported herewith is the third recorded instance of reduplication of the stomach.

Enterogenous cysts are closely related embryologically to congenital diverticula. Meckel's diverticulum occurring as a failure of closure of the omphalomesenteric duct is the commonest form of congenital diverticulum. Cysts occurring in this region usually represent remnants of this embryological structure. These cysts, wherever they occur in the intestinal wall, may be intermuscular, submucosal or subserosal, or may occur as a reduplication anatomically similar to the normal gastro-intestinal tract which they duplicate, as in the case of reduplication of the stomach reported by Ladd and Gross. In isolated instances, cysts have lost their connection with the wall of the intestine and may occupy a position between layers of the mesentery somewhat removed from the parent gut. The uniform characteristic of these cysts is that the structure of the cyst wall resembles the intestinal wall from which it was derived. Occasionally, intra-cystic pressure or inflammatory changes may produce variations in the epithelial lining of these cysts.

Symptoms produced by these cysts in the intestinal tract vary with their location and are usually manifested by evidence of obstruction, infection, or both, and rarely by the presence of a palpable mass. Most often symptoms are produced which lead to recognition of these cysts at laparotomy in early infancy, but our case of reduplication of the stomach was 27 years of age. The preoperative diagnosis of such a cyst is extremely unlikely, although a presumptive diagnosis may be made rarely in the presence of a palpable mass with obstructive symptoms.

Treatment of enterogenous cysts has varied widely with different observers and it may be said that each cyst presents a problem which must be solved individually. Removal of a cyst without entering the bowel lumen is frequently impossible because it is so intimately attached to the wall of the bowel. Resection of the bowel and its contained cyst is usually the method of choice. In cysts of the duodenum, resection or total removal may be impossible because of the danger of damage to the common or pancreatic ducts. Attempts to drain these

* Read before the Southern Surgical Association, White Sulphur Springs, W. Va., December 9, 1948.

cysts externally have usually resulted in failure because of their tendency to recur. External drainage of such cysts was attempted in both of the cases of enterogenous cysts of the stomach previously reported and apparently was successful in the case of Ladd and Gross. The method of internal drainage suggested by Gardner may be the method of choice in some instances.

The case reported by Ladd and Gross was that of a seven-year-old girl whose reduplication of the stomach closely simulated the adjacent normal stomach. Symptoms which led to a laparotomy were a vague gastro-intestinal disturbance and roentgen-ray evidence of encroachment on the normal stomach

FIG. 1.—Roentgenogram of stomach demonstrates prominence of mucosal pattern with evidence of extrinsic pressure on duodenal cap.

lumen along the greater curvature. Treatment consisted of marsupialization of the mass with subsequent débridement and packing with gauze. The case of Ferraro occurred in a six-months old child. Symptoms consisted of the presence of a mass in the left upper quadrant which was incised when the child was six weeks old. The operative area continued to drain a watery fluid until laparotomy was performed at the age of six months. At operation the cyst was removed from the stomach along with a small portion of the stomach wall.

The wound healed well, and recovery from the cyst was apparently satisfactory. The child died later of worm infestation and malaria.

CASE REPORT

F. I. F. (No. 24675—Columbia Hospital), age 27, was admitted to the Columbia Hospital October 9, 1947. He stated that he had been suffering abdominal discomfort for six months prior to admission. Pain was not severe but consisted of a tugging sensation just to the right of the umbilicus (at the top of an old right rectus incision for appendectomy). This tugging sensation had been present in some degree since appendectomy in 1942 but was more severe lately. His discomfort was aggravated by activity. A feeling of fullness in the stomach and slight nausea after eating were prominent, but other digestive disturbances were minimal. At intervals since the onset

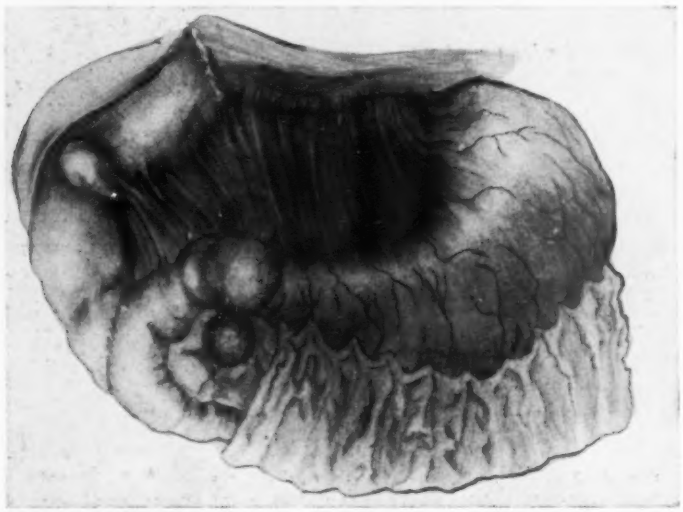

FIG. 2.—Illustrates position of cyst within stomach wall. Portion of cyst imbedded in stomach wall is identified by dotted outline.

of symptoms he had run a low-grade fever. All efforts to trace down the cause of this fever were fruitless. He had lost 13 pounds since the onset of symptoms.

Family History: Negative.

Past History: Tonsillectomy in 1932. Appendectomy in 1942 for acute appendicitis.

Laboratory Examinations: Total white and differential counts had been repeatedly normal. Urinalysis was normal. "Fever tests" and smears for plasmodia had been repeatedly negative. Roentgen-ray examination revealed the presence of an obstruction in the region of the duodenum in the opinion of one radiologist. Repeat roentgen-ray examination produced the following report: (Fig. 1)

> "Examination of the stomach, duodenum and esophagus demonstrates a pronounced prominence of the gastric and duodenal mucosal pattern with a slight diminution in peristaltic vigor. No hernia or ulcer can be demonstrated. The duodenal cap is flattened but its contour is not that of ulcerative disease. Opinion: Generalized hypertrophic gastroduodenitis of marked degree. To be considered are the possibilities of lymphoblastoma and allied conditions."

Physical Examination: Essentially negative except for slight tenderness just to the right of the umbilicus at the upper end of a lower right rectus incision.

Operation: On October 10, 1947, exploratory laparotomy was performed. The cavity was entered through an upper midline incision. Adhesions to the abdominal wall were absent. Thorough exploration was carried out, and no pathologic condition was detected except at the lower end of the stomach. At this point a cyst was found on the anterior aspect of the stomach near the pylorus (Fig. 2). Palpation of the pyloric end of the stomach revealed that the major portion of the cyst was buried deep in the gastric wall or was actually intraluminal. The cyst could not be emptied by gentle compression. Edema of tissues adjacent to the cyst evidenced a low-grade inflammatory process. A window was made into the stomach, and the cyst was found to be beneath the mucosa. The portion of the cyst within the stomach wall was dissected out (Fig. 3). This wound was closed with 0 chromic catgut reinforced with No. 40 cotton. The window into the stomach lumen was closed by the same method.

FIG. 3.—Intact cyst after removal. Four-fifths of larger portion of cyst was imbedded in the stomach wall.

Pathologic Report: "Received an hourglass-shaped structure removed from the stomach wall. It consisted of two cysts which connected one with the other. One cyst was 5 cm. in length and 3½ cm. in diameter. The other cyst was 6½ cm. in length and 4 cm. in diameter. The two cysts were tense with fluid material which could be pressed from one cyst to the other. On gross sections, the walls appeared to be fibrous tissue in character, and the contents were yellowish in color, very thick and mucinous and sticky in character. The inner walls were finely granular in appearance and yellowish in color.

"Microscopic sections of this tissue show that the walls of the cysts are made up of involuntary muscle fibers and fibrous connective tissue. The cysts are poorly lined by a single layer of small, atrophic, deep-staining epithelial cells. No inflammatory reaction is seen in the tissue. There is no evidence of any malignancy in the sections.

"It appears that this double cyst is an outpouching of a part of the stomach wall which has subsequently lost all direct communication with the stomach cavity.

"Diagnosis: Double (hourglass) cyst of the stomach."

Postoperative Course: Uneventful except for the development of mild thrombophlebitis on the tenth postoperative day. Follow up report of recent date reveals that he is completely relieved of symptoms and considers himself entirely well.

DISCUSSION:

1. The third recorded case of enterogenous cyst of the stomach is reported.
2. Unique features of this case are:
   a. The fact that he was 27 years old before his disease was discovered.
   b. Production of low-grade temperature by inflammatory reaction within the cyst.
   c. The presence of chronic interference with emptying of the stomach.

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DISCUSSION.—DR. THOMAS D. SPARROW, Charlotte, N. C.: In more than 9000 pediatric admissions to the Charlotte Memorial Hospital during the past eight years, we have encountered two cases of reduplication of the intestinal tract. One of these cases was a girl eight years of age. She was admitted to my service and presented such findings that I feel they are worth recording. The child was brought to the hospital because one month previously, she had had a frank hemorrhage of bright blood from the bowel, which clotted after passing. The parents stated that since infancy she had complained of intermittent cramping pains about the umbilicus and on frequent occasions had passed blood in the stools. At six months of age she vomited a considerable amount of blood and, on one or two occasions, she coughed up bright red blood. At that time two bronchoscopic studies were made. It was thought that the bleeding was due to tuberculosis of the peribronchial glands; however, tuberculin tests were negative. At 13½ months of age, she vomited blood and blood was noted in the stools. When three years of age her weight

was 27 pounds, although she was anemic and was passing tarry stools. At four years of age, because of the pain in the abdomen, her appendix was removed.

On admission to the hospital she appeared to be a perfectly normal child of eight years of age. Physical examination was entirely normal and x-ray studies of the chest and intestinal tract were normal. She was quite anemic and her stools definitely contained blood. The Department of Pediatrics was unable to find any definite cause for bleeding and a tentative diagnosis of Meckel's diverticulum with ulceration was made. She was prepared for operation by giving her several small transfusions.

At operation the terminal ileum was found to be entirely normal but, on exploration of the intestinal tract, a reduplication of the jejunum was encountered. It began about 10 centimeters along the jejunum. At its distal end, the reduplication or diverticulum communicated with the jejunum. At its proximal end there was a large, bulbus-like structure, buried between the folds of the mesentery. The mesenteric vessels could be seen crossing the reduplication before entering the jejunum. Forty-eight centimeters of the jejunum, including the reduplication, was resected and a side-to-side anastomosis was performed. The child made an uneventful recovery and was allowed to leave the hospital on the eleventh day. (slides)

The first slide shows the normal jejunal mucosa. The second slide shows the mucosa of the reduplication which closely resembles that of the stomach. In the bulblike structure of the proximal end of the reduplication there was an ulcer, which was the source of the hemorrhage and which closely resembled the ordinary peptic ulcer.

Gross has described the symptoms produced by these lesions under three headings: Obstruction of the alimentary canal by regional external pressure; pain produced by distention of the cystic mass; and hemorrhage caused by interference with the intestinal blood supply, leading to sloughing of the intestinal mucosa. We believe the pain and hemorrhage in the cases seen in our hospital were probably due to ulceration of the gastric-like mucosa. The symptoms may be indistinguishable from those of Meckel's diverticulum with ulceration and hemorrhage. In those cases diagnosed as Meckel's diverticulum in which the lesion is not found, a thorough investigation of the intestinal tract should be made in search for a possible duplication.

THE MANAGEMENT OF PATIENTS WITH BLEEDING FROM THE UPPER GASTRO-INTESTINAL TRACT WITH BUFFER AND THROMBIN SOLUTION*

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IN RECENT YEARS the concept with regard to treatment of bleeding from the upper gastro-intestinal tract has changed. Fortunately, within the past 15 years, progress has been made which has led us away from the old idea of starvation and heavy sedation in these cases. The contributions of Andresen[1] and Muelengracht[2] were an advance over the watchful-waiting method of dealing with bleeding peptic ulcers in that some nutrition and materials were supplied to counteract the ill effects of the acid of the stomach, but development of operative methods for stopping hemorrhage was not stimulated. Within the past ten years there has been a tendency on the part of surgeons to consider the importance of control of hemorrhage rather than to wait for the hemorrhage to stop because of lessened blood volume and the resulting decrease in blood pressure.

In instances in which the hemorrhage from an ulcer was not great and the patient was in good condition, the Andresen or Muelengracht type of treatment was successful. Once the hemorrhage stopped and an adequate thrombus was formed in the bleeding vessel, repeated small feedings and rest in bed were usually sufficient to decrease the acid and to permit healing to take place. In cases in which the bleeding was vigorous or the patient was unable to withstand the resulting hemorrhage, death occurred. All too often if surgical intervention was resorted to, it was carried out upon patients who had become exsanguinated through continuous bleeding for several days or, what in general appeared to be worse, through repeated severe hemorrhages. The surgical mortality under these conditions could not be expected to be low.[3] The experiences undergone during World War II revealed that a patient could stand fairly massive acute hemorrhage if sufficient quantities of blood were replaced immediately. There were those who thought that if a patient was bleeding excessively, the most direct and efficacious method of handling the problem was to ligate the bleeding vessel. This has always been a primary principle in the control of hemorrhage—to ligate the bleeding vessel or stop the hemorrhage by pressure, especially if the bleeding is from a surface wound.

The only difficulty encountered in bleeding from the gastro-intestinal tract is lack of accessibility to the bleeding area. Since principles are very much the same regardless of the site of bleeding, many surgeons believe the best approach to the problem of a patient bleeding from the upper intestinal tract

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is a direct and early one. With adequate blood available for replacement during the operative procedure, a sufficient margin of safety is afforded to permit the surgeon not only to stop the bleeding but in many instances to carry out definitive treatment for the peptic ulcer. Two deterrents exist to prevent wide acceptance of the dictum that all bleeding peptic ulcers require immediate surgical intervention. One of these is that in the majority of cases the bleeding stops spontaneously; the other is that it is not always possible to localize the site of the bleeding or to determine accurately its cause or its extent.

From a review of the literature[4, 5, 6, 7, 8] relating to the treatment of bleeding peptic ulcers, several important points have been stressed. In the older age group the mortality from bleeding from the upper gastro-intestinal tract is more serious than in younger individuals. This is as might be expected. Many have related this increased mortality to specific reasons, such as the changes incident to age in the blood-vessel wall. A much more plausible explanation would take many more of the factors of age into account. Some authors have been inclined to the view that patients over 40 should have operative intervention for bleeding from the upper intestinal tract, while others feel that the lower limit for surgical intervention is the age of 50. It is readily seen from a study of any large series that mortality may result from bleeding peptic ulcer in any age group.

This would lead us to the belief that more important criteria are the ability of the patient to withstand hemorrhage and the amount of hemorrhage that is present. It seems obvious to us that no sharp dividing line can be drawn, and that the patient must be considered individually.

One other fact that seems clear to us is that patients who have repeated massive hemorrhages do poorly as compared with those having a single episode of bleeding. From our own experience we find that long-continued bleeding likewise adds a hazard for the patient. In the case either of long-continued bleeding or repeated hemorrhages, surgical intervention is quite likely to be resorted to, and in these individuals surgery is more hazardous than in those who suffer from a single massive hemorrhage.

Of the cases of upper gastro-intestinal bleeding reported in the literature, duodenal and gastric ulcers are the commonest causes. Bleeding from esophageal varices, gastric malignancy or other causes form only a small percentage of the total number.

It is difficult to obtain reliable information for most of the series reported in regard to the amount of blood lost. Some have attempted to determine this on the basis of hemoglobin determination or red-cell count. In cases in which blood transfusions are not given, the hemoglobin level, especially if known before bleeding occurred, serves as a rough index but is not a reliable means of determining the amount of blood a patient has lost.

About three years ago we were confronted with a serious problem in relation to a patient who had had bleeding almost continuously for four days. He had been supported during this interval by blood transfusions which were

inadequate to maintain his hemoglobin above a level of 6.7 Gm. per 100 cc. The patient was not in very good general condition, the problem of anesthesia seemed hazardous, and because of his size and build, operation appeared difficult. Under the conditions presented, operative intervention seemed to us to be an almost hopeless gesture. Since one of our number was working on a fundamental problem relating to thrombin and the bleeding seemed not too vigorous, it appeared worth while to attempt to stop the hemorrhage by the use of topical thrombin.[9, 10, 11] It was obvious that if the thrombin were to work it would be necessary to neutralize the hydrochloric acid in the stomach, and for this purpose copious amounts of phosphate buffer were used. The bleeding stopped promptly and the patient responded immediately to blood transfusions and made an uneventful recovery.

Since that time we have used thrombin and buffer in over 100 cases of bleeding from the upper gastro-intestinal tract. Variations in the use of this method have been employed. In the first 64 cases the buffer and thrombin were administered by mouth or inserted in the stomach through a Levin tube. In the first group of cases, attempts were made to stop the hemorrhage without other considerations. It soon became obvious to us that the method could be used not only to stop the hemorrhage but also to determine whether or not the hemorrhage was controlled. With the tube in the stomach and with gentle suction applied, it was possible to tell whether bleeding was continuing, for we noted in the cases in which the bleeding had stopped that the material aspirated from the stomach contained very fine, brown granules of clotted blood, whereas in the case of continued bleeding, large, loose clots having a different color and texture were noted, and in some instances fresh blood was removed from the suction tube.

The method which we have found most effective in the management of hemorrhage from the upper gastro-intestinal tract is as follows. A Levin tube is passed through the nose into the patient's stomach. The stomach is then washed with buffer solution or saline, and following this, 50 cc. of seventh-molar phosphate buffer* is introduced into the stomach. This is allowed to remain for five minutes. An additional 50 cc. of phosphate buffer is introduced, and with it 10,000 units of topical thrombin.† The tube is then clamped for a half hour. During this period blood studies are made, and if the patient appears to be suffering from serious blood loss, a transfusion is given. After 30 minutes the clamp is removed from the Levin tube and slow, gentle suction is applied. For this purpose we have utilized a pump with a valve mechanism which permits of low suction, not to exceed a foot of water. The material removed from the suction tube is observed through the glass connector. If the bleeding has stopped, the material removed usually appears finely granular and

* 20.4 Gm. of di-sodium phosphate in a liter of water.
1.95 Gm. of di-hydrogen potassium phosphate in 100 cc. of water.
These are then mixed, producing 1,100 cc. of seventh-molar of phosphate buffer, pH of 7.6.

† The thrombin for this study was kindly supplied by Parke-Davis & Company.

light-colored; if bleeding is continuing, fresh, blood-stained material can be seen in the tube. If there is no further evidence of bleeding from the stomach, 50 cc. of buffer solution is introduced every half-hour, allowed to remain a half-hour and then aspirated. The buffer may be applied by slow drip. This process is carried on for several days. In cases in which bleeding continues, the process is repeated. If, however, the bleeding appears to be uncontrolled by thrombin administration, other measures for controlling hemorrhage are resorted to.

TABLE I.—*Cause of Bleeding*

		Controlled, Recurred				
	Controlled	Then Controlled by Thrombin	Operation	Not Controlled	Not Controlled	Died from Bleeding
Duodenal ulcer	36		4			
Peptic ulcer—site unknown	15			1		1
Bleeding—site unknown	7			1		1
Gastric ulcer	6	3				
Esophageal varices	7			2	1	3
Malignancy	4					
Miscellaneous	12		1			
Total	87	3	5	4	1	5

There is a question which cannot always be answered relating to whether the bleeding is coming from an ulcer of the stomach or duodenum, or whether it is due to esophageal varices. More recently, in cases of doubt, we have utilized the technic developed by Patton,[12] which we have found will effectively control bleeding from esophageal varices and at the same time permit us to tell whether the bleeding is from the esophagus or below. In rare instances it has been possible for us to determine that the bleeding was from esophageal varices because the patient vomited blood at the instant that clear material was coming from the stomach through the Levin tube.

We have analyzed the data from the first 100 cases in which thrombin and buffer were used. The data were collected at the time the patient was in the hospital as it was recognized that the use of this material was on an experimental basis. There was no attempt to select cases. All cases in which there was more than minimal bleeding from the upper gastro-intestinal tract were studied. Cases in which there was evidence of peptic ulcer on the basis of history but in which there was no localization of the site of the ulcer either by roentgen-ray or operative findings, were classified as peptic ulcer. Only those cases in which there was proof of the site of the ulcer were classed as duodenal or gastric ulcers. In the case of bleeding from esophageal varices, we required fairly reliable proof before classifying them as such. Such proof consisted of demonstration of the varices by roentgenogram, esophagoscopy, postmortem examination or the presence of cirrhosis of the liver without evidence of the presence of ulcer. Cases in which we could not be reasonably sure of the

source of the bleeding during the patients' stay in the hospital were classified as "site unknown." A miscellaneous group of cases in which the source was reasonably certain were as follows: hemorrhagic gastritis 6, retroperitoneal sarcoma 1, congenital short esophagus 1, hemorrhage from gastric suture line 2, gunshot wound postoperative 1, chemical gastritis 1, pseudodiverticulum of duodenum 1. Table I indicates the distribution of the cases as to diagnosis. Eighty-seven were controlled by the use of thrombin buffer alone. In eight additional cases the hemorrhage was controlled by the use of thrombin buffer but it recurred. In three of these eight cases it was possible adequately to control hemorrhage again by the use of buffer, but in five it was felt that operation was a more effective means of controlling the hemorrhage. There were four cases in which bleeding recurred after having been controlled with thrombin and further treatment was ineffective. These patients were not operated upon, and the hemorrhage was not controlled. One other case died from massive hemorrhage in which the bleeding was at no time controlled.

TABLE II.—*100 Cases Treated with Thrombin and Buffer*

Hemoglobin Levels	Stopped		Stopped, Recurred, Then Controlled	Stopped, Recurred, Not Controlled With Thrombin	Not Controlled at All
	1st Rx	Multiple Rx			
0–2	1	1			
2–4			1		
4–6	7	6		2	2
6–8	13	6		2	1
8–10	21	10	1		
10–12	8	1			
12 and above	6	7	1	3	
Total	56	31	3	7	3

An attempt was made to obtain information relative to the amount of bleeding. It was not possible to determine the amount of bleeding by measurement of the vomitus because in many instances blood was lost into the lower gastro-intestinal tract, the vomitus was mixed with food and gastric juice and, in most instances, blood had been lost before the patients were seen by us. It is well known that a study of hemoglobin levels is an unreliable measurement of the amount of blood lost, not only because of the factor of concentration but also because it is quite impossible to determine in these cases what the level of the hemoglobin was before the bleeding started. In addition, it was not always feasible to obtain hemoglobin determinations before transfusion was given since it is customary in our hospital to begin transfusion on exsanguinated patients as soon as they arrive in the emergency ward. The majority of the hemoglobin levels were made in these cases after one or more transfusions had been given. So far as the hemoglobin determinations are concerned, the majority of these patients give no indication of the actual amount of blood lost. The data are presented as the only means at hand, other than clinical evaluation, for estimating the amount of blood lost. We

recognize that this is a very rough estimate and in most instances, the hemoglobin levels were higher than the clinical appearance of the patient indicated. As can be seen from Table II, the hemoglobin levels gave no indication as to whether or not it would be possible to stop the hemorrhage by one or multiple doses of thrombin or whether the thrombin would be entirely ineffective. One might expect that the greatest number of deaths would occur in those patients who presented the lowest initial hemoglobin levels. Yet two of the patients whose initial hemoglobin levels were too low to be determined survived, while another with a hemoglobin of 13 continued bleeding and died. The hemoglobin levels in the table represent initial determinations. The data do not represent the lowest hemoglobin levels obtained from the patient, nor do they indicate the amount of hemoglobin available to the patient just before death.

Table III illustrates the ages of our cases—for the most part, in terms of decades. While we recognize the fact that the series is small, it is worthy of note that there is approximately the same incidence of deaths from hemorrhage

TABLE III.—*Age Incidence G. I. Tract Hemorrhage—100 Cases*

Age Incidence	6 Months to 1	5 to 20	20 to 30	30 to 40	40 to 50	50 to 60	60 to 70	70 to 80	81 to
Death from hemorrhage (5)				2			2	1	
Death from other causes (7)				1	1	3	1	1	
Total deaths (12)				3	1	3	3	2	
	86 White 14 Negro			88 Male 12 Female					

in the 30 to 40 age group as is found in the 60 to 70. There were no deaths from hemorrhage in the age group 40 to 60. We are quite certain that the five cases listed as deaths from hemorrhage occurred from loss of blood. In patients who died from other causes, loss of blood played a minor role, if it contributed at all. One patient died following a gastrectomy performed several weeks after he had recovered from his bleeding episode. The gastrectomy was performed to cure his ulcer, and the patient died in cardiovascular collapse with a hemoglobin of 13 and without evidence of postoperative hemorrhage. One patient died from severe diffuse peritonitis, another from duodenal fistula, and another death was due to severe uremia unassociated with the bleeding period. One patient had severe diabetes mellitus and cirrhosis of the liver; another had widespread metastases of carcinoma in the liver and died from pneumonia; while another died in delirium tremens. In none of these seven cases did any fresh hemorrhage precede death.

Despite the fact that the population of our hospital is predominantly Negro, the majority of patients who suffered from bleeding of the upper gastrointestinal tract were white, there were 86 white people in this series and 14 colored. Eighty-eight of the patients were males, while 12 were females.

DISCUSSION

Despite the fact that this method was being developed during this study of 100 consecutive cases of upper gastro-intestinal bleeding, the data indicate that the method is a valuable adjunct in the treatment of upper gastro-intestinal hemorrhage.

While the data suggest that thrombin and buffer is useful in controlling hemorrhage from the upper gastro-intestinal tract, our experience leads us to the conclusion that it should not be considered as a sole form of therapy. In many cases this treatment is ineffective for stopping bleeding and in such cases early operative intervention is necessary.

The procedure is important as an aid in differentiating those patients in whom the hemorrhage is controlled from those who require surgical intervention to stop the hemorrhage. The use of the method in conjunction with the Patton tube has been useful in determining whether a patient is bleeding from the esophagus or from below the cardia of the stomach.

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DISCUSSION.—DR. BYRNE M. DALY, Detroit: I would like to thank the Association for the privilege of participating in this meeting. We are often asked concerning preparation of the buffer solution. This solution is made by dissolving 20.4 Gm. of disodium phosphate in a liter of water, and 1.95 Gm. dihydrogen potassium phosphate in 100 cc. of water. It is done in this manner because of solubility. They are mixed, producing 1100 cc. of seventh molar phosphate buffer with a pH of 7.6. We prefer to use this buffer

because of its availability, non-toxicity and the fact that it is a clear solution enabling us to evaluate when bleeding has stopped. Other substances may be used such as sweet milk, soda bicarbonate and the commercial antiacids, but we have found that the buffer is more effective. (slides)

In determining the effect upon patients we have studied 35 hospitalized patients. This slide represents what we consider between the best and poorest results in this study. We first aspirated the contents to determine the pH by the Beckman glass electrode and in this case it was just a little above 2. At this point 30 cc. of buffer were given and five minutes later the pH was determined; you can see the marked rise. At this point about 180 units of topical thrombin was administered in 30 cc. of buffer and the pH and the units of thrombin were determined at five minute intervals, with results as seen.

Our treatment, as mentioned in the paper, varies somewhat. Our latest addition, which we hope will decrease mortality even more, is the addition of a Patton tube. This tube, as you see, is approximately 3 feet in length. It has three air vents, two of which are utilized; one air vent goes directly to the first balloon, the second goes to the larger one, and there is a complete lumen through the tube which allows aspiration of the stomach. In cases of suspected esophageal varices the tube is placed through the nose down into the stomach and the first balloon is dilated. The balloon is then pulled back against the cardia of the stomach and the second balloon is inflated, which will be in the esophagus, and we can tell whether this is adequately placed by applying traction; if the first balloon is not steady the tube will be pulled back. If it is firmly fixed the tube is taped at the nares. If bleeding stops after inflation it can be assumed to be from esophageal varices. If aspiration shows continued blood loss, the source can be suspected to be below the esophagus, and thrombin treatment instituted.

We feel that this addition to treatment will enable us to cut down the mortality in our next 100 cases.

AN APPRAISAL OF PANCREATODUODENAL RESECTION: A FOLLOW-UP STUDY OF 61 CASES*

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AND
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THE OPERATION of pancreatoduodenal resection has been performed for 13 years, since it was first reported by Whipple[1] and associates in 1935. Large numbers of patients have been operated on during this period. Their course has been followed for a sufficient time to permit evaluation of the procedure when employed for carcinoma of the head of the pancreas, carcinoma of the ampulla, carcinoma of the duodenum and carcinoma of the lower end of the common bile duct. The operation as described by Whipple was the first attempt to apply the general principles of radical cancer surgery to these serious and relatively inaccessible lesions. A few large series of cases have been reported by Whipple,[2] Orr,[3] Waugh and Clagett,[4] Waugh,[5] Bartlett[6] and Cattell.[7]

In the six-year period from August 1942 to August 1948, 165 patients with carcinoma in the region of the head of the pancreas were observed at the Lahey Clinic, and on 56 of these a pancreatoduodenal resection was performed. During this time five additional patients had pancreatoduodenal resections for benign disease, giving a total experience for pancreatoduodenal resection of 61 cases. Careful follow-up studies have been made on every one of the resected cases.

Basing our data on a review of this experience, we have attempted to answer certain logical questions that have arisen, which can be stated as follows: (1) What patients are suitable for resection? (2) Should a one-stage or a two-stage operation be employed? (3) Is it essential to anastomose the pancreatic duct? (4) Can carcinoma of the ampulla be cured? (5) Is it worth while to resect carcinoma originating in the head of the pancreas? (6) Can a reasonable operative mortality be obtained? (7) Does pancreatoduodenal resection offer sufficient palliation in extensive cases to be worth while?

Too few series of cases have been followed for the generally accepted period of five years to judge curability on this basis. In our own series, only 12 patients were operated on more than five years ago. Orr,[3] in 1945, collected 103 cases from the literature, including 11 personal cases, and of this group found that no patient survived over three years. Waugh,[5] in reporting a follow-up study of 30 cases in which operation was performed at the Mayo Clinic, reported that one patient who had had a carcinoma of the ampulla survived for three years. Bartlett[6] reported 25 cases from the Massachusetts General Hospital and found one survival of five years.

* Read before the Southern Surgical Association, White Sulphur Springs, W. Va., December 9, 1948.

† Trainee, National Cancer Institute.

From August 1942 to August 1948 at the Lahey Clinic, 165 patients with carcinoma of the head of the pancreas, ampulla of Vater, duodenum and lower end of the common bile duct were treated (Table I). Fifty-six patients were submitted to pancreatoduodenal resections, an operability rate of 34 per cent. During this time two additional patients with carcinoma arising in a hyperfunctioning pancreatic adenoma were submitted to local resection. These two patients have previously been reported on by Allan and Marshall.[8] Most of the remaining patients had exploratory laparotomies and palliative procedures such as cholecystjejunostomy.

TABLE I.—*Pancreatoduodenal Resection—Operability (1942-1948)*

Patients with carcinoma	165
Pancreatoduodenal resections	56 (34%)
Local resections	2

Fifty-six cases of pancreatoduodenal resection for carcinoma were divided according to the location of the lesions (Table II). In 20 the lesion arose in the ampulla. In two the lower end of the common duct was the primary site, while four had a primary lesion of the duodenal mucosa near or about the ampulla of Vater. A somewhat larger number, 30, apparently arose in the head of the pancreas, usually thought to be in the duct of Wirsung. In this latter group the process was frequently diffuse, making the point of origin impossible to determine. Three patients are submitted to pancreatoduodenal resection with an operative diagnosis of carcinoma of the head of the pancreas; in these the lesion was found to be benign. These patients were excluded from the group of 56 operated on for carcinoma and included in the five operated on for benign disease. The other two were operated on with the diagnosis of benign disease.

TABLE II.—*Pancreatoduodenal Resection—Pathology*

Carcinoma of ampulla	20
Carcinoma of head of pancreas	30
Carcinoma of duodenum	4
Carcinoma of common duct	2
Total	56

Among the patients submitted to resection were both favorable and unfavorable cases. Particularly in our earlier experience, some extensive carcinomas of the head of the pancreas were included in which it was known at the conclusion of the operation that all the malignancy was not excised. These included patients with involvement of the superior mesenteric vessels, invasion of the portal vein and retroperitoneal extension. Regional node involvement, likewise, was frequently demonstrated, particularly at the inferior angle of the common bile duct and the duodenum, as well as those nodes superior to the duodenum in the gastrohepatic omentum. Our experience with these cases of more extensive malignant disease has been unsatisfactory and led us to discontinue resection in

these unfavorable cases. It is now our opinion that when local invasion or metastases to lymph nodes are present, operation should not be advised.

The operation of pancreatoduodenal resection may be done in one or two stages. Whipple,[1, 2, 9, 10] in his extensive experience, began with a two-stage operation and now feels that the one-stage operation can be done. Trimble,[11] Orr,[3] Waugh[5] and Brunschwig[12] likewise favor the one-stage operation. In our experience with 61 pancreatoduodenal resections (Table III), at the Lahey Clinic, 25, or 40 per cent, were done in one stage. This includes all five resections for benign lesions. Thirty-six patients, or 60 per cent, were operated on by a two-stage operation, 10 of these having had their first stage done elsewhere. The first-stage operation which we recommend is a cholecystjejunostomy utilizing a long antecolic loop of jejunum. The second stage is

TABLE III.—*Pancreatoduodenal Resection—Operation*

One-stage operation (including 5 benign)	25 (40%)	4 deaths
Two-stage operation*	36 (60%)	5 deaths
Total	61	

* 10 patients had first stage done elsewhere.

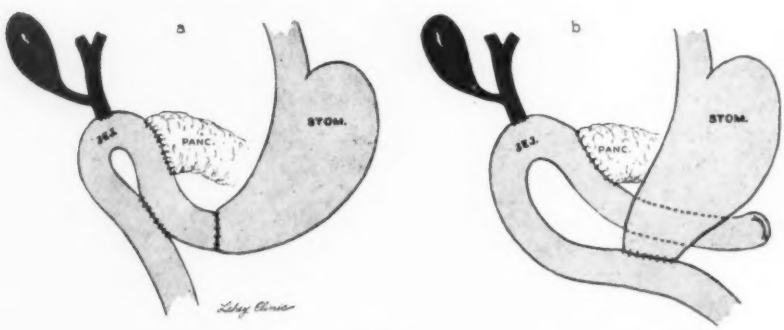

FIG. 1

delayed for from two to three weeks, during which time the condition of the patient greatly improves. In our experience, this procedure does not add appreciably to the technical difficulties of the resection. We believe that the employment of the two-stage operation has enabled us to extend the operation to patients who would not otherwise be suitable risks for such a major procedure. Furthermore, it permits surgeons who do not choose to carry out the radical procedure to perform a first-stage operation at the time of their exploration. From our own experience, we believe that the employment of the two-stage operation has been the most important factor in maintaining a low mortality.

The two-stage operation is employed in patients with long-standing jaundice, in those with marked enlargement of the liver and in the group represent-

ing the poorest surgical risks. If the gallbladder has previously been removed or is unsuitable for the anastomosis, choledochostomy is satisfactory for a first stage. It adds considerably to the technical difficulty of the resection, but may be the wise procedure.

The technic of operation will not be presented in this paper. The operation that we usually employ has recently been presented.[13] The one-stage operation which we prefer has all anastomoses in an antecolic position and they consist of

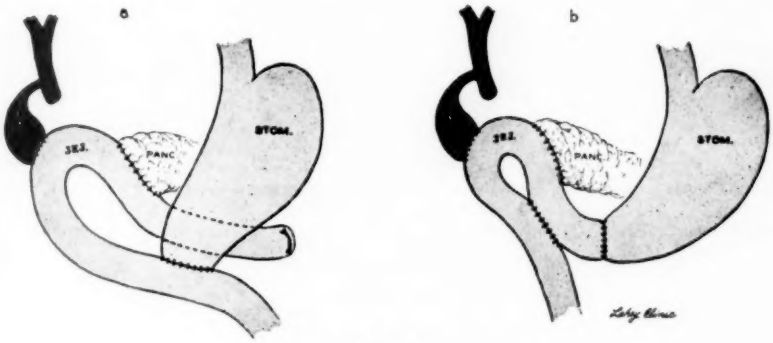

FIG. 2

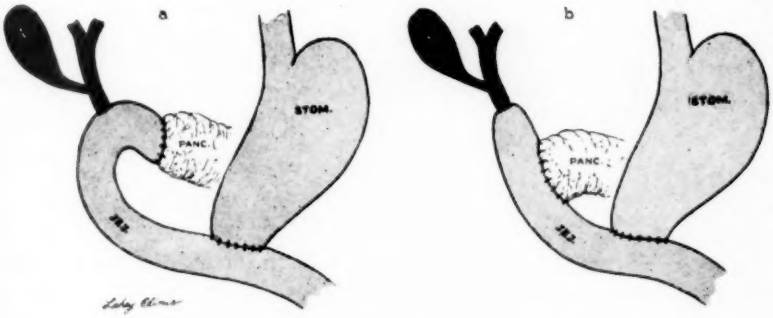

FIG. 3

end-to-end gastrojejunostomy, entero-enterostomy, pancreatojejunostomy and choledochojejunostomy (Fig. 1 *b*). The entero-enterostomy may be avoided by implantation of the stomach distal to the pancreatic and biliary anastomoses and then become an end-to-side gastrojejunostomy (Fig. 1 *a*). In the two-stage operation, the common duct is turned in (Fig. 2 *a* and *b*) or if its division is close to the entrance to the cystic duct, it is implanted in the jejunum beside the cholecystjejunostomy. Anastomosis of the end of the jejunum to the common

duct with implantation of the pancreas and stomach below the biliary anastomosis, as employed by Whipple and Waugh, has been utilized (Fig. 3 *b*). This may be reversed so that the end of the jejunum is joined to the pancreas (Fig. 3 *a*).

The operative mortality following pancreatoduodenal resection has varied in the reported series from 11 to 45 per cent. In the 56 resections for carcinoma in our series, there were eight deaths, a mortality of 14.3 per cent. In addition to this, there were five resections for benign disease, with one death, or 20 per cent. This one death occurred in a patient who was operated on with the mistaken diagnosis of malignant disease. In Table IV the operative deaths are recorded, based on the site of the lesion. Of the nine patients who were submitted to resection for carcinoma of the ampulla in one stage, there were

TABLE IV.—*Pancreatoduodenal Resection—Operative Mortality*

	Cases	Deaths	Per Cent
1-stage carcinoma, ampulla	9	0	
2-stage carcinoma, ampulla	11	1	
	20	1	5.0
1-stage head of pancreas	9	3	
2-stage head of pancreas	21	2	
	30	5	16.7
1-stage carcinoma, duodenum	1	0	
2-stage carcinoma, duodenum	3	2	
1-stage carcinoma, common duct	1	0	
2-stage carcinoma, common duct	1	0	
Total	56	8	14.3

no deaths. Eleven had a two-stage operation, with one death. In the total series of 20 patients with carcinoma of the ampulla, there was one death or a 5 per cent mortality. It must be remembered that these are the most favorable lesions.

There were nine patients with carcinoma of the head of the pancreas who had resection in one stage with three deaths, and 21 were done in two stages with two deaths, a total of 30 with five deaths, or a mortality rate of 16.7 per cent. Four patients with carcinoma of the duodenum had resection, with two deaths. These occurred in the three patients submitted to a two-stage operation. A one- and a two-stage operation were each done for carcinoma of the common duct, without a fatality.

In the interpretation of these results it should be appreciated that the patients who were the most serious risks, those with the greatest interference with liver function, were operated on in two stages. We feel that this mortality rate of 14.3 per cent for malignant disease, 14.8 per cent including benign disease, is evidence in favor of a two-stage operation for the deeply jaundiced individual.

The causes of death in fatal cases are seen in Table V. Fatal gastro-intestinal hemorrhage occurred in two. The site of bleeding could not be determined. Generalized peritonitis was found in two patients. In one the pancreatic anastomosis had separated. In this patient, metastases were found in the retroperitoneal region and also in the lungs. One patient died of surgical shock with possible transfusion reaction; this was the patient who had resection with a mistaken diagnosis of cancer. One of the patients early in the series died as a result of sepsis with liver abscess occurring nine weeks after operation.

TABLE V.—*Pancreatoduodenal Resection—Fatal Cases*

Gastro-intestinal hemorrhage	2
Peritonitis	2
Liver abscess	1
Shock	1
Hepatorenal syndrome	1
Cerebral thrombosis	1
Coronary thrombosis	1

Death followed one-stage resection in a case with an hepatorenal syndrome and associated renal suppression. The cause of death in another was cerebral thrombosis in a poor-risk patient with arteriosclerotic heart disease and hypertension. Coronary insufficiency and thrombosis caused death during operation in a 77-year-old man with a favorable lesion of his ampulla.

The duration of life following the onset of cancer in the region of the head of the pancreas is quite short. In an earlier report,[14] we found in 56 consecutive patients who were operated on prior to 1935, in whom cholecystjejunostomy was performed, that 75 per cent were dead within six months of

TABLE VI.—*Pancreatoduodenal Resection—Five-year Survival, 1942-1943*

1942	2	1*	6 years, 2 months
1943	10	2*	5 years, 7 months

Recurrent Cases

1 (carcinoid)	lived 4 years, 7 months
1*	lived 3 years, 4 months
1*	lived 3 years, 2 months

50% (6) lived 3 years or more
25% (3) living and well

* Carcinoma of ampulla.

the operation. A review of our patients submitted to pancreatoduodenal resection definitely demonstrates that life can be prolonged when the operation is performed in suitable cases and that some patients may be cured. Only a small group in this series was available for a five-year follow-up study. During 1942, two resections were done, and during 1943, 10 resections were performed, making a total of 12 patients whose course has been followed for five years. One patient with carcinoma of the ampulla is living and well after six years and two months; the second is in good condition for five years and seven months, and a third, five years and five months after operation. All had adeno-

carcinoma of the ampulla of Vater without extension. Of the patients who had recurrent disease and subsequently died, one who had carcinoid of the ampulla lived four years and seven months and two others with carcinoma of the ampulla without metastases lived three years and four months and three years and two months, respectively. Thus, in this small series of 12 cases, three, or 25 per cent, of those submitted to resection five years or more ago are living and well, while six, or 50 per cent, lived three years or more.

It seems worth while to report the three-year survival rate in our series. For the years 1942 to 1945, 27 of the 56 patients had resections. Of these, eight, or 30 per cent of the group, lived three years or more. The two patients with carcinoma of the duodenum surviving resection lived two years and eight months respectively. The two with carcinoma of the common duct, lived three years and five months and one year and nine months, respectively.

There were 30 patients with carcinoma of the head of the pancreas submitted to resection, with five fatalities. This left 25 patients, all of whom have

TABLE VII.—*Pancreatoduodenal Resection—Three-year Survival, 1942-1945*

1942	2	1
1943	9	5
1944	6	0
1945	10	2
1942–1945	27	8 (30%)

had follow-up studies. Eighteen were found to be dead of recurrence, with an average duration of life of 11 months after resection. The longest duration of life was 19 months. Seven patients are still living, as follows: three years and seven months, two years and three months, one year and three months, one year, and three patients have been followed for less than one year.

This relatively short survival time after pancreatoduodenal resection for carcinoma of the head of the pancreas is the most discouraging finding in all of our experience with these cases. It is a similar observation to that of the other recorded series. It must be admitted that no patient with carcinoma of the head of the pancreas has yet been cured or survived five years or more. While many of these patients have a smooth recovery and are quite comfortable for a number of months, the duration of their life following resection hardly justifies such a major procedure since satisfactory palliation might have been procured by a sidetracking operation, such as cholecystjejunostomy, for the relief of obstructive jaundice. In the light of our present experience, we must modify the operative procedure or abandon radical surgery for carcinoma of the head of the pancreas. We have observed rapid peritoneal dissemination with carcinomatosis in patients in whom the line of resection passed through malignant tissue, and it is quite possible that in some unfavorable cases we have hastened death rather than delayed it. We can certainly assume that resection for extensive cases of carcinoma of the head of the pancreas or those with local direct extension or regional metastases should no longer be consid-

ered for resection. Even with apparently very favorable lesions confined to the duct of Wirsung, we have seen recurrence as early as nine months. An isolated observation by Cole[15] may explain early recurrence with favorable lesions. He found malignant cells free in the obstructed duct of Wirsung and it is possible that dissemination of cancer occurs by cutting across the duct, with the escape of pancreatic fluid. Before discontinuing radical pancreatectomy for carcinoma of the head of the pancreas in favorable cases, we wish to suggest the employment of total pancreatectomy in which this possible complication could be avoided. It has not yet been employed under these circumstances in our clinic. According to our present understanding of this problem, the employment of total pancreatectomy in early carcinoma of the head of the pancreas offers the only chance of a possible improvement of these results.

We have undertaken a survey of the nonfatal complications as well as physiologic studies on patients after resection but these will not be reported in this paper. An excellent study of 10 cases has been recently reported by Wollaeger[16] and others.

From our experiences with 61 pancreatoduodenal resections, including 56 for carcinoma, and five for benign disease, the following points have been answered. (1) The operation is technically feasible as it has been developed. (2) With proper selection of cases and the employment of a two-stage operation in selected cases, the operative mortality can be maintained at a reasonable level, one similar to that for other gastro-intestinal cancers. (3) Physiologic functions so far as the gastro-intestinal tract and pancreatic and liver function are concerned can be established and maintained. (4) Carcinoma of the ampulla can be cured in an appreciable number of cases. (5) Pancreatoduodenal resection should be confined to favorable lesions. (6) Carcinoma of the head of the pancreas has not yet been cured. (7) The operation of pancreatoduodenal resection as now employed is suitable for carcinoma of the ampulla. Pancreatoduodenal resection for carcinoma of the head must be modified or discarded.

CONCLUSIONS

A series of 61 pancreatoduodenal resections performed at the Lahey Clinic has been reported. Fifty-six were employed for carcinoma in the region of the pancreatoduodenal area and five were performed for benign disease.

Twenty patients with carcinoma of the ampulla were operated on, with one death, a 5 per cent mortality. Thirty patients with carcinoma of the head of the pancreas had resections, with five deaths, a mortality rate of 16.7 per cent. Fifty-six resections for carcinoma were done, with eight deaths, or 14.3 per cent. Five resections for benign disease were done, with one death, 20 per cent. Sixty-one resections were followed by nine operative deaths, 14.8 per cent.

Twenty-five patients, 40 per cent, had pancreatoduodenal resection as a one-stage procedure. Thirty-six, 60 per cent, were operated on in two stages.

Of 27 patients having pancreatoduodenal resections for carcinoma, eight (30 per cent) survived three years or more.

Of 12 patients followed for five years or more, three show no evidence of recurrence. All had carcinoma of the ampulla of Vater. The longest period a patient was followed was six years and two months.

Pancreatoduodenal resection should be reserved for those patients with favorable lesions.

Carcinoma of the ampulla may be cured by pancreatoduodenal resection.

Carcinoma of the head of the pancreas has not been cured by pancreatoduodenal resection. A more extensive operation, such as total pancreatectomy, should be carried out or resection for this condition should be abandoned.

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DISCUSSION.—DR. MALCOM THOMPSON, Louisville, Ky.: One of my medical friends has said that his most fervent prayer is to be delivered from a surgeon who is always talking about his one case. As Doctor Cattell has shown us, follow-up reports of seven years' duration upon cancer of the ampulla of Vater are infrequent, so I will risk my friend's censure and solicit your indulgence by being brief. (slides)

This shows a photomicrograph of the specimen, pronounced cancer by two pathologists, one of whom reviewed the slide a few weeks ago.

This shows the method of reconstruction. The patient was in the hospital when Ridgeway Trimble's paper appeared, in the November, 1941 issue of *Surgery, Gynecology and Obstetrics*. Without the knowledge gained from his paper I am sure I would not have had the confidence to proceed. Our technic was exactly as described by him with minor changes as follows: In attempting to bring the common bile duct into the jejunum through counter incision by grasping the duct with a hemostat, the wall was so fragile that it tore, so two guide sutures were placed in each lateral wall of the duct. These were brought through a small incision into the jejunum on needles. The needles then pierced the jejunal wall a slight distance from the opening and the sutures tied upon the serosal surface. In this manner the common duct was anchored into the jejunum as shown. There was not sufficient duodenohepatic ligament to buttress the area of entrance of the duct into the jejunum, so a small piece of detached omentum was sutured around the junction. Also, there was not sufficient duodenohepatic ligament to suspend the jejunum properly so, a few centimeters distally, it was suspended by two sutures to the edge of the liver to relieve tension upon the sutures anchoring the duct.

The patient was jaundiced for five weeks before operation. One-stage excision was performed on November 7, 1941. You might note the date, for had *S. G. & O.* been late that month we would have been content with simply a palliative shunt, or perhaps later a second stage excision. He has been well for seven years and at present there are no signs of recurrence.

This color slide shows the opened specimen a few minutes after completion of the operation. As you see it is composed of the distal portion of the stomach, the pylorus and the proximal three-fourths of the duodenum. The tumor, 2 centimeters in diameter, can readily be seen at the ampulla and, posteriorly, there is a portion of the head of the pancreas with a small segment of the common duct.

The fact that this man has gone for seven years without chills or fever, without jaundice, without any major digestive disturbances and with the biliary anastomosis distal to the gastric and no attempt to implant the duct of Wirsung will, I am sure, be of interest to Doctor Cattell and to others of you who by your originality and large experience have contributed so much to treatment of this condition.

DR. RICHARD B. CATTELL, Boston (closing): This is a most excellent result in the case reported by Doctor Thompson, and is a long period of survival in carcinoma of the ampulla. I am sure he is wise in recording this striking result with a seven-year survival, because there are too few long follow-ups in these cases.

RESULTS OF TREATMENT OF PATIENTS WITH HYPERTENSION BY TOTAL THORACIC AND PARTIAL TO TOTAL LUMBAR SYMPATHECTOMY, SPLANCHNICECTOMY AND CELIAC GANGLIONECTOMY*

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ESSENTIAL HYPERTENSION or hypertensive vascular disease is by common usage a term applied to a large group of patients having elevation of systolic and diastolic blood pressure. Cause of hypertension in these patients cannot be explained by known clinical or laboratory diagnostic methods. Damage to the arteries supplying the brain, the heart, the kidneys and other organs or abnormal function of these organs is seldom evident in early stages of the disease process.

Patients who present themselves when blood pressure is moderately elevated and before occurrence of serious vascular or organic damage usually are treated by medical methods including restriction of physical and emotional activity, reassurance, sedation, reduction of weight and various drugs or diets. They must be examined periodically to determine whether or not blood pressure levels increase, vessels of the retina evidence vascular damage or renal or cardiac function alters. Eventually, serious complications occur in many.

Patients who present themselves late in the hypertensive disease process evidencing serious organic damage may also be treated by a medical program, although in some, at least, delay during conservative treatment may permit rapid occurrence of complications. Eventually, most patients with hypertension die of the disease. Usually at some stage physician and patient alike consider the possibility of supplementing medical treatment by sympathectomy.

Decision regarding indications for sympathectomy is difficult because of the variety of opinions regarding the cause of hypertension and the effect of various treatments. A variety of possible etiologic factors has been developed experimentally. Contributions of many investigators have been previously reviewed and acknowledged.[1-4]

Most of these etiologic factors should not be amenable to sympathectomy. The renal factor is one of these. It consists of a vasoconstrictor and vasopressor substance, angiotonin (Page) or hypertensin (Houssay), circulated through the blood as a result of liberation of renin during renal anoxia. This

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enzymatic humoral process apparently explains the Goldblatt hypertension produced by constricting renal arteries. Many experiments indicate that neither production nor action of this substance would be altered by sympathectomy. Another factor, arteriolar sclerosis, developing as a result of some unexplained degenerative or metabolic process, would not be directly altered by denervation of blood vessels.

Another possible etiology, neuroendocrine in nature, has been attributed to two similar sequences. One, Selye's excessive adaptive reaction,[5] postulates stimulation in the sequence of frontal lobe, anterior pituitary and adrenal cortex, with production of excessive corticoid hormone. The other, Heinbecker,[6] postulates that functional influences stimulate the frontal lobes, which in turn affect the hypothalamic nuclei, neural hypophysis and anterior pituitary eosinophil cells, producing an excess of a cortical hormone. These in turn might constrict efferent glomerular renal arterioles, producing renin which, with anterior pituitary and cortical hormones, might cause hypertension. Either sequence is assumed as a complete chain of neurohumoral reactions independent of the sympathetic nerves. Heinbecker suggests, however, that epinephrin liberated as a result of the activity of the sympathetic nerves supplying the adrenal medulla might increase the irritability of the frontal lobes and thus augment their reaction to functional influences.

Several recent developments have suggested additional causes of hypertension. Schroeder[7] has described a pressor substance from human blood, more active in hypertensive than in normal patients. Shorr[8] has described a balance between a vasoexcitatory material (V. E. M.) and a vasodepressor material (V. D. M.), originating respectively from kidney and liver, which modify vascular response to epinephrin and might, if not properly balanced, be a factor in hypertension. Shipley, Helmer and Kohlsteadt[9] report a vasopressor substance occurring in hypotensive cats which gives a sustained increase of blood pressure in nephrectomized animals and seems different from renin.

Any of the several etiologic factors described above, if present in a patient with hypertension, would presumably weigh against a decision for sympathectomy. Experiments, however, with the Heymans' neurogenic hypertension produced by excision of the carotid sinuses and division of the cardio-aortic depressor nerves indicate that if a counterpart exists in a hypertensive patient, treatment by sympathectomy would be effective. Studies of this form of experimental hypertension and review of experiments by others[10-12] indicate that either splanchnicectomy or upper thoracic sympathectomy alone does not appreciably alter the hypertension, but that total sympathectomy does. Moreover, even after total sympathectomies in dogs, hypertension may partially return as some regeneration of nerve occurs. Because of the encouragement offered by these experiments and with a concept that a neurogenic etiologic factor might be present in essential hypertension, total sympathectomy in patients was attempted through a transthoracic approach in May, 1940.[13] The celiac and stellate ganglia were included in the sympathectomy to insure completeness of visceral denervation and to minimize regeneration. Although

complete denervation, as judged by sweating tests, was not obtained, results have led to the continued use of the procedure.

It is possible that, of the several etiologic factors presented above, the neurogenic factor might initiate and perpetuate the disease process in some patients, arteriolar sclerosis, renal, neuroendocrine and other mechanisms occurring later. Also, it is entirely possible that additional factors now receiving only a little attention or now unrecognized may further complicate the complex disease process.

Decision regarding indications for sympathectomy in patients with hypertension is also difficult because of the difference in methods of studying and reporting results and the variety of operations employed. Methods of reporting results of sympathectomy for hypertension have varied widely, many authors changing method or operative technic frequently. Results in patients followed for several years are seldom quoted.

Operations are of two general types. The first is the splanchnicectomy. Its development, including anterior root ramisection, 1930, Adson and Heuer; subdiaphragmatic approach to sympathetic nerves and branches, 1932, Craig and Adson; supradiaphragmatic approach, 1933, Peet; celiac ganglionectomy; transabdominal approach, Crile; lumbodorsal approach, 1938, Smithwick, and transthoracic approach, 1940, Grimson, has been reviewed, comparing the results of procedures and acknowledging the opinions of authors.[4] Since this review, Poppen,[14] 1947, further modified the thoracolumbar approach by resecting part of the seventh rib to gain access to the sympathetic chain as high as the fourth thoracic ganglia. Regardless of the upper level of interruption of the sympathetic nerves to somatic segments of the body, significant denervation of viscera is accomplished by each of the above operations only in the splanchnic area. Cardiac, pulmonary, cerebral, upper thoracic, arm and head areas remain supplied by sympathetic nerves from the stellate and remaining upper thoracic ganglia. The second type of operation for sympathectomy, total thoracic and partial to total lumbar sympathectomy, splanchnicectomy and celiac ganglionectomy, using a transthoracic approach, 1940, Grimson,[13] denervates thoracic viscera, head, neck, arms and chest, as well as abdominal viscera supplied by the splanchnic nerves and, to a varying extent, lower abdomen, groin and legs.

In spite of the confusion described above concerning etiology, operative results and technic, most physicians today accept sympathectomy. Decision regarding indication or contraindication for surgery and type of sympathectomy is usually left to the surgeon and is a matter for individual judgment. Our experiences with splanchnicectomy performed in 45 patients of another series have led to an opinion in agreement with that of Findley[15] and others that although results are occasionally excellent, usually they are temporary or poor. Also, it seems evident that the effect of this procedure is largely one of palliation. It is the purpose of this paper to present results of adding denervation of thoracic viscera, upper body, head, neck and limbs to splanchnicectomy that

surgeons may consider how results of this near total sympathectomy compare with those obtained by various forms of splanchnicectomy.

Material. Operations to be reported were undertaken for 113 patients treated between June, 1940, and May, 1948. Each had a persistent elevation of systolic and diastolic blood pressure, not decreasing with medical treatment and not significantly decreasing during a week or more of hospital study preceding operation. Major complications of hypertension present before operation were hemiplegia in 19 patients, hypertensive retinopathy with hemorrhages and exudates in 38 and with papilledema in 11, definite decrease of renal function in 9, marked enlargement of the heart in 15 and definite abnormality of the heart as judged by electrocardiogram in 65. No patient had infarction of the myocardium and there was only one elevation of nonprotein nitrogen, since these were considered contraindications to operations. Also, no patient had a hypertension considered mild or not progressive by medical consultants. Ages varied from 15 to 50 years; the average was 36. There were 46 males and 67 females.

Only two patients did not have symptoms attributable to hypertension. Symptoms occurring in the remainder were occasional headache only in 11; mild headaches, fatigue, dizziness, dyspnea, blurring of vision, palpitation, precordial pain or nervousness in 23; and severe multiple symptoms in 77. It should be emphasized that each of these patients had a moderately severe or severe form of hypertension. They were selected for operation when recommended by majority opinion of consultants and not on a basis of decrease of blood pressure after sodium amytal[12] or with sympatholytic drugs.[16] Also, these patients usually had been followed during treatment by a medical program lasting for several years before operation, occasionally followed for about a year and only rarely for a few months.

Method of Operation. Operations usually were accomplished in two stages performed three weeks apart. During each operation a lateral incision was made over the third rib, four or five inches of the rib was excised, and the upper thoracic cavity was exposed transpleurally. Through the open chest, the pleura then was incised directly over the sympathetic chain, following which dissection and mobilization of the stellate ganglion, the upper six to eight thoracic ganglia and the origin of the splanchnic nerve was accomplished. The freed chain was dropped into the lower chest and the upper incision closed. A second lateral incision was made over the tenth rib, permitting excision of six or seven inches and entry into the lower portion of the thoracic cavity. The chain and splanchnic nerve previously mobilized were picked up and freed down to the diaphragm. Here a transverse incision was made through the reflection of the pleura onto the diaphragm and through the posterior attachment of this structure. This permitted anterior and downward retraction of the diaphragm and retroperitoneal visualization of the first and often the first and second lumbar ganglia. One or both of these ganglia were removed. Traction upon the splanchnic trunk and separation of the muscular fibers of the diaphragm permitted mobilization of the greater portion of the celiac

ganglia, division of its branches and communications and partial or complete excision. Exploration of the adrenal glands, when desired, was accomplished through a small incision through the diaphragm into the retroperitoneal and periadrenal space.

Since effusion and rarely bleeding occurred after operation and since a chest drain has not caused any recognized ill effects, a stab wound was routinely made between the eighth and ninth ribs and a No. 32 Fr. Pezzer catheter brought out through it. The incision through the tenth rib bed was then closed. A sterile two-bottle, bed level to floor, gravity suction was connected to the catheter. Three weeks were allowed between this operation and the second stage, a similar procedure through the opposite chest, in order that recovery of respiratory function on the first side be fairly complete. Occasionally, patients received a third transabdominal operation to complete denervation of the lower trunk and limbs. Two patients, because of the seriousness of their disease, had bilateral transthoracic splanchnicectomies in two stages through the tenth rib followed a few months later by upper thoracic sympathectomies, also in two stages and through the fourth ribs.

The specimen of excised chain always included stellate and all twelve thoracic ganglia, splanchnic nerves, part or all of the celiac ganglia and the first or first and second lumbar ganglia.

Method of Study. Each patient was examined employing standard cardiovascular and renal technics and observed by cardiovascular roentgenologic, psychiatric and urologic consultants. Examinations were performed during the four to ten days in the hospital before the first operation and were repeated during the second week following the last stage. With few exceptions patients were again hospitalized for four to ten days 3½ months after sympathectomy and subsequently at yearly intervals for six years. Occasionally special examinations including blood volume, cardiac output, blood viscosity, renal blood flow and effects of posture were carried out. Details of the method of study will be given as the results are reported.

RESULTS OF SYMPATHECTOMY

Extent of denervation early and late after operation. The surface area of the body denervated by sympathectomy was determined by inspection and palpation in each patient, by Richter's neurodermometer methods[17] in many and by an iodine starch heat test in 21.

The iodine starch test has been used for calculation of area of denervation. It was performed shortly after sympathectomy and again during subsequent admissions to the hospital at intervals, one to seven years later. After sweating under a heat cradle photographs were taken of the entire body, front and back. Percentages of body surface were obtained by comparing photographs with a standard surface area chart. The average of the surface area denervated in 21 patients soon after sympathectomy was 77 per cent; the range was from 54 to 98 per cent. Residual sweating after operation usually was greatest about the groin and thigh. Illustrative photographs have been published.[2, 13] The

average of tests made one to seven years, average three years, after sympathectomy in 17 patients was 61 per cent; the range was between 39 to 85 per cent. Recovery of ability to sweat occurred in irregular patches usually on the trunk and legs and occasionally on the arms. The distribution of these patches of sweating was an irregular pattern and resembled that seen in nerve regeneration. Ray[18] recently reported neurodermometer studies after "total sympathectomy" in 14 patients and described similar results. Return of sympathetic activity occurred; he attributed it to a process of readjustment taking place during the first three months after incomplete denervation. It should be recognized that sweating and neurodermometer tests record activity of cholinergic nerves distributed segmentally along with the adrenergic sympathetic fibers and supplying the body surface.

It has not been possible to test the completeness of interruption of adrenergic or true sympathetic nerves to the head, extremities or trunk or to abdominal and thoracic viscera. During operation the celiac ganglia or at least their upper and lateral portions were removed. This was done to insure the division of lesser splanchnic branches which might otherwise be overlooked and to diminish the possibility of regeneration of adrenergic vasomotor nerves to abdominal viscera. Also, the stellate ganglia were excised to insure cardiac and pulmonary denervation and to guard against regeneration. Horner's syndrome occurred bilaterally and with rare exception has persisted. Excision of these ganglia eliminates cell stations which might otherwise offer connections for myelinated preganglionic fibers growing out from rami and permitting effective regeneration and activation of unmyelinated post ganglionic adrenergic fibers.

A definite change of heart rate occurred after sympathectomy. The heart rate under basal conditions, as recorded by the electrocardiograph, averaged 76 before sympathectomy and 59 a few weeks afterward. Two to six years later the average was 58. The rates four to seven and one half years after sympathectomy showed no further recovery, the average being 58. These persistent low rates might indicate failure of regeneration to the heart.

Operative Mortality. Four of the 113 patients died in the hospital shortly after sympathectomy (Table I). Three of these four deaths occurred among the first 19 patients treated, and each of the three patients exhibited findings now conventionally accepted as contraindications to sympathectomy. These operations were performed in 1940 and 1941 to test the effectiveness of the new procedure in otherwise hopeless or late stages of the hypertensive disease process. The first patient, a 48-year-old male, had all of the findings associated with malignant hypertension, including elevation of blood urea and nitrogen. He developed pneumonia two weeks after the first transthoracic operation, became uremic during treatment with sulfathiazole and died 47 days later. The second patient, a female of 33, had had a severe hypertension for 11 years, complicated by occurrence of several cerebral accidents. At the time of operation she was confined to bed. Examination revealed findings of hemiplegia, severe encephalopathy and also malignant hypertensive retinitis with papilledema.

There were recurring periods of unconsciousness before and between the two operations. Respiratory arrest occurred one day after the second stage. Blood pressure remained around 140/90 during several hours of artificial respiration just preceding death. The third operative mortality occurred in a 43-year-old male. He had had many episodes of nocturnal dyspnea. Examination of the retina revealed advanced arterial sclerotic disease and areas of venous thrombosis and macular degeneration. After the second operation blood pressure was reduced to normal for 56 hours and then respiratory arrest occurred. Autopsies of the last two patients revealed evidence of increased intracranial pressure. The arteries of the circle of Willis showed advanced sclerotic degeneration.

TABLE I.—*Survival Statistics of Patients Treated by Subtotal to Total Paravertebral Sympathectomy.*

Follow-Up Period — 1 to 9 Years — Average 3½ Years

Operative mortality	
Respiratory arrest	2
Uremia	1
Myocardial infarction	1
	—
Total	4
Death since operation	
Cerebral, vascular	6
Cardiac	3
Phlebitis	1
Cushing's	1
Pregnancy	1
	—
Total	12

Ratio Living During Each Year Period	Now Living
8 years plus	7 of 9
7 to 8 years	2 of 8
6 to 7 years	3 of 3
5 to 6 years	3 of 4
4 to 5 years	7 of 9
3 to 4 years	16 of 19
2 to 3 years	24 of 25
1 to 2 years	35 of 36
Total	97 of 113

Total now dead	16
Total now living	97
Total number	113

The fourth patient who died shortly after sympathectomy was a male of 37 years of age with a severe hypertension of two years known duration. During six months prior to operation he had noted "tightness in the chest" after mild exercise. This was relieved after a few minutes of rest. Two electrocardiograms revealed only left axis deviation. Death occurred on the third day after the second sympathectomy. Autopsy revealed marked arteriosclerosis of the coronary arteries. Occlusion of one artery by a fresh thrombus had caused necrosis of the myocardium. This is the only operative death occurring during the last six years or among the last 94 patients.

Survival Statistics. (Table I.) Twelve of the 113 patients treated by sympathectomy died during the one to eight and one-half year period of postoperative observation. Four of these twelve obtained no symptomatic improvement. Two died two months after operation with cerebral accidents and one with myocardial infarction. The fourth developed thrombophlebitis and a marked neurosis after the first stage of the sympathectomy and left the hospital. Death occurred two months later at home and cause could not be determined.

The remaining eight patients dying after the operation had described some symptomatic improvement. Two were of unusual interest. One had a diagnosis of "Cushing's syndrome" established before operation. The sella turcica was normal by roentgenogram. Sympathectomy was completed at the time of exploration of the abdomen and either side of the chest searching for tumor. Biopsy of the adrenal glands was performed during the abdominal and each transthoracic operation. After completion of the sympathectomy blood pressure remained at normal levels for one year and symptoms of dizziness, headache and palpitation were relieved. Other characteristic changes and symptoms of "Cushing's syndrome" progressed, however, even though medical treatments including roentgen-ray therapy to the pituitary gland were employed. Osteoporosis led to multiple fractures and collapse of vertebrae. Tuberculosis of the spine and later acute hematogenous miliary tuberculosis then developed. Death occurred 33 months after sympathectomy. At autopsy, although the hypophysis was grossly normal, a small basophilic adenoma was found during microscopic examination. The second patient of special interest was a girl, 15 years of age at the time of sympathectomy whose blood pressure had been reduced to normal during 15 months. She then became pregnant, concealing this from the family for seven months. Convulsions then occurred and she was hospitalized elsewhere with a blood pressure of 230/160. Death occurred one day later.

Of the remaining six patients dying during the period of postoperative observation, four had cerebral accidents 14, 16, 17 and 36 months after sympathectomy. The remaining two patients died suddenly of heart failure, one 46 months and the other 26 months after sympathectomy. The last case is of interest. She had had a bilateral supradiaphragmatic splanchnicectomy one year and two months before completion of the sympathectomy and had obtained little improvement and no reduction of pressure with this procedure. There was definite clinical improvement following a three-stage paravertebral sympathectomy but no reduction of pressure. The patient was rehabilitated sufficiently to do light work until three months before death. Progressively increasing cardiac decompensation then developed. Terminally intestinal volvulus occurred. Autopsy revealed generalized sclerotic and thrombotic arterial vascular disease.

Ninety-seven of the original 113 patients are now living one to eight and a half years after operation, an average survival time of 36.5 months. (Table I.)

It is evident that most deaths after operation occurred among the eight patients treated seven to eight years ago. At this time the operation was employed for patients in an extremely advanced stage of the disease. Of the six patients who were operated upon during this year and subsequently died, two were operative mortalities described above, another had the "Cushing's syndrome" and the remaining three developed cerebral vascular accidents 16, 17 and 36 months after operation. In general, considering the type of patients treated, it is believed that the above survival periods are more than satisfactory.

Effect upon Blood Pressure. Blood pressures were obtained at intervals

before and after operation in the office and also during periods of four to ten days in the hospital. Readings were obtained while patients were supine and usually also while sitting and standing. Generally, office readings taken in the supine position were somewhat higher than those taken routinely four times a

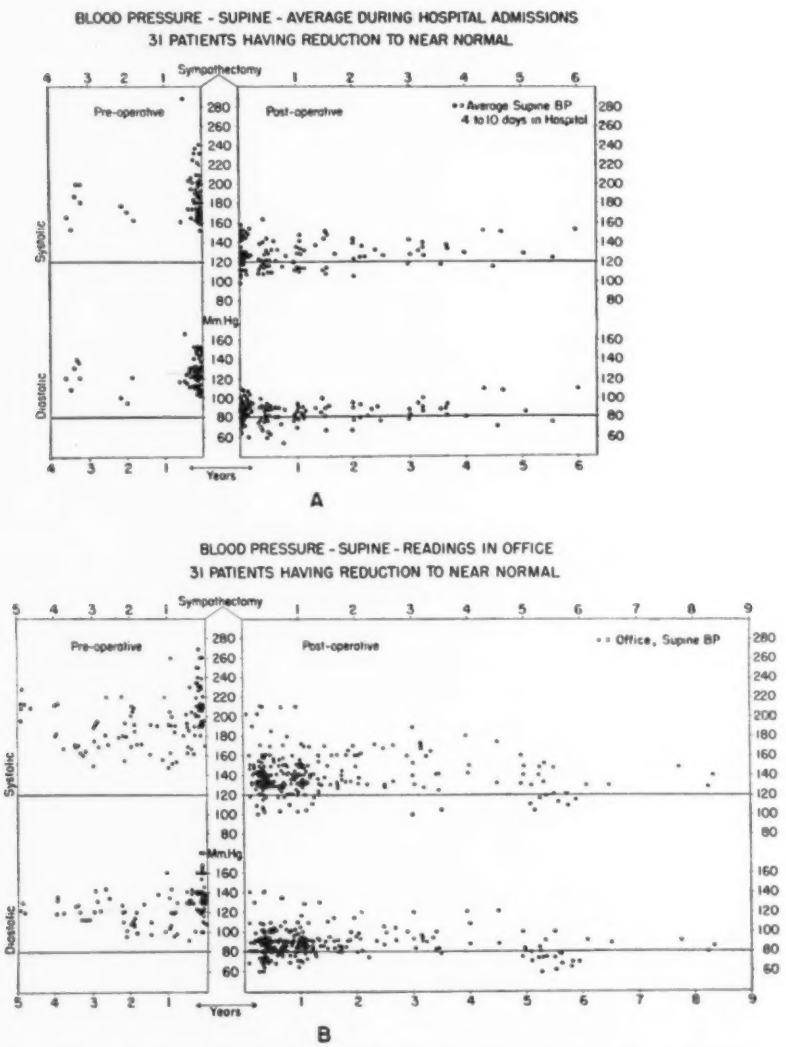
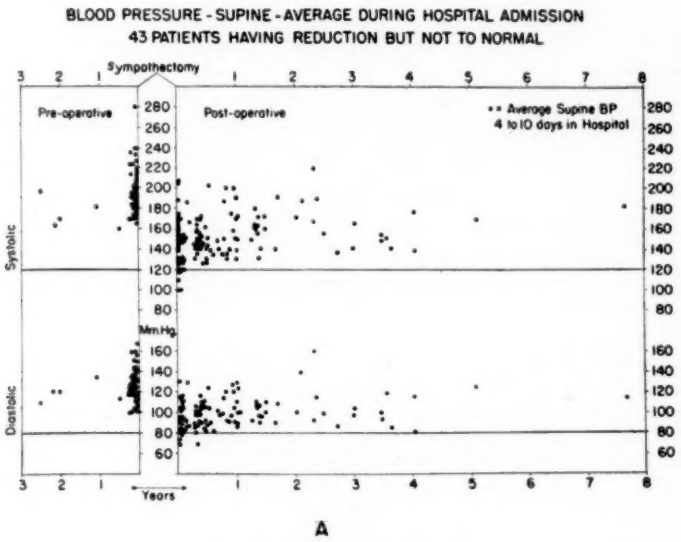


FIG. 1.—Scattergraphs present blood pressures of 31 patients considered as having reduction to near normal values as judged by average supine pressures during admissions to the hospital (A). Office readings of the same patients in the supine position are presented in (B). Progressive elevation of pressures during the years before operation has ceased afterward.

day during hospital admissions. After operation a postural hypotension occurred, blood pressure decreasing with upright posture and with exercise. During the first several months, standing often produced dizziness. Subse-

quently, little or no dizziness occurred. The postural hypotension with few exceptions persisted during periods of observation as long at 8½ years. It was not associated with tachycardia since heart and adrenal glands were denervated.



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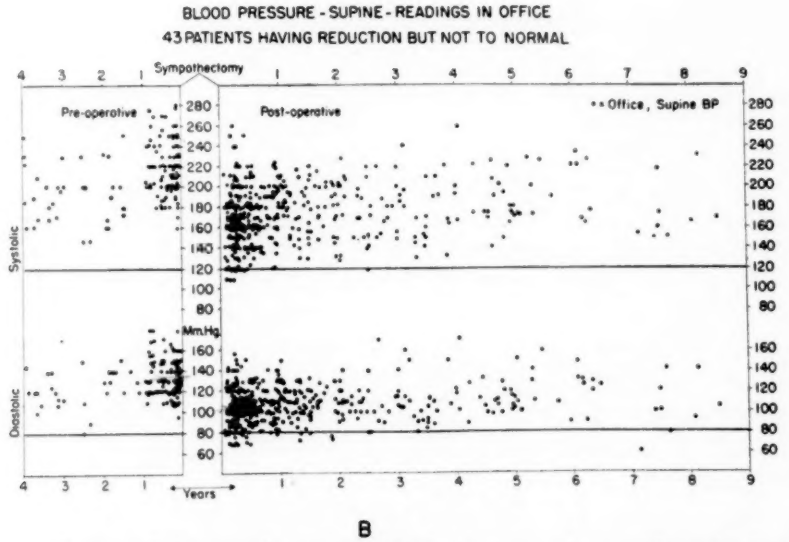

B

FIG. 2.—Scattergraphs present blood pressures of 43 patients having reduction but not to normal as judged by hospital averages (A). Office readings of these patients (B) indicate progressive increase of blood pressure before operation and a plateau during the years afterward.

Master charts plotting the course of the blood pressure were kept for each patient. Since the readings in the hospital fluctuated less than those obtained in the office, the hospital readings were chosen as the basis for determining

effect of sympathectomy upon blood pressure. Supine readings during each admission to the hospital but excluding those during cold pressor, sodium amytal and other tests were averaged and indicated as a single point on the

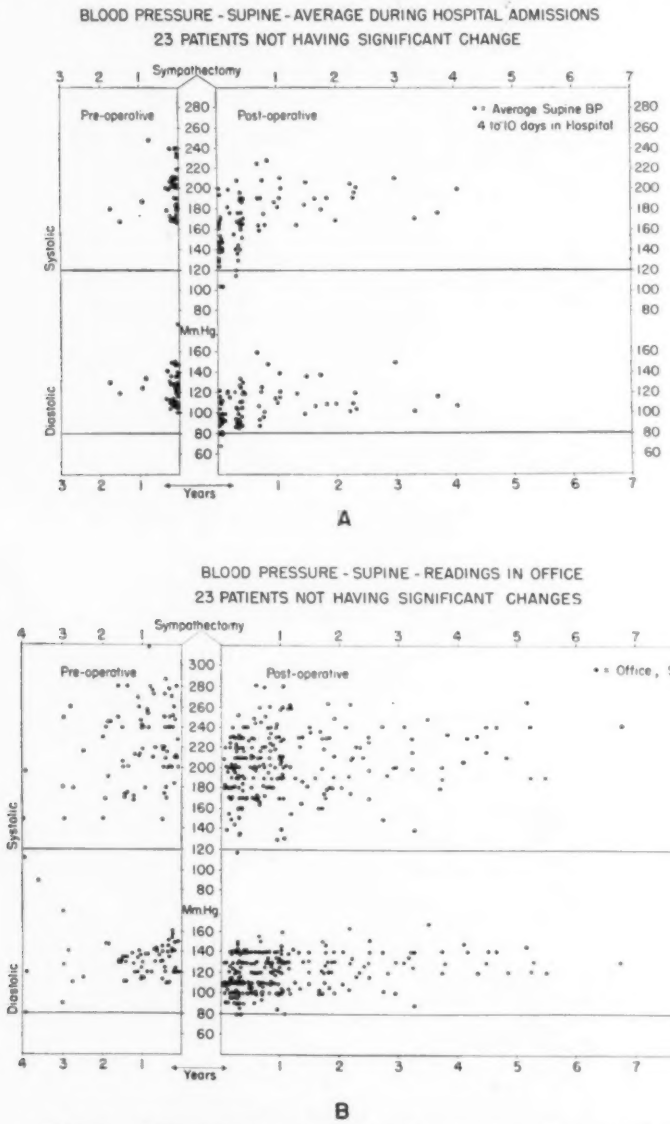

FIG. 3.—Scattergraphs present blood pressures of 23 patients having no significant reduction of blood pressure as judged by averages during hospital admissions (A) or readings in the office (B). Pressures during the years after operation have not increased.

patient's master chart. The master chart of each of the 97 patients now living was then surveyed to determine whether the over-all record indicated reduction of blood pressure to near normal, reduction but not to normal, or no definite reduction. On the basis of this individual survey, 31 patients were

considered as having reduction of blood pressure to near normal. For presentation, a scattergraph has been prepared (Fig. 1) showing a dot for each hospital average on each patient (A) and for each office reading of each patient (B). On the same basis, 43 patients were considered as having reduction but not to normal (Fig. 2, A and B). Similarly, 23 patients were considered as having no significant reduction (Fig. 3, A and B). Examination of individual master charts usually reveals the same upward trend of blood pressure before sympathectomy which is evident in these scattergraphs but always the same arrest of upward trend or plateau after sympathectomy.

Age at the time of sympathectomy of the 31 patients with near normal blood pressure presented in Figure 1 varied from 17 to 46 years, average 32. The age of patients in Figure 2 with reduction but not to normal varied from 20 to 48, average 38 years. The age of patients without significant reduction (Fig. 3) varied from 27 to 50, average 38 years.

TABLE II.—*Symptoms Before and After Sympathectomy, 97 Patients Now Living.*

	Nervousness	Blurring Vision	Fatigue	Dizziness	Headaches	Precordial Pain	Palpitation	Dyspnea
	Number of Patients							
A. Before operation								
1. 31 with B. P. reduced to normal	13	13	8	15	28	10	11	18
2. 43 with some reduction	18	14	16	29	41	11	20	18
3. 23 with no reduction	8	9	9	11	20	12	13	15
Total 97 patients	39	36	33	55	89	33	44	51
B. After operation								
1. 31 with B. P. reduced to normal	0	1	8	11	6	0	1	3
2. 43 with some reduction	3	5	8	14	16	3	0	8
3. 23 with no reduction	4	5	7	5	13	1	2	8
Total 97 patients	7	11	23	30	35	4	3	19

Known duration of hypertension among the 31 patients with blood pressure reduced to near normal varied from 1 to 10 years, average 5.1; of the 43 with some reduction, 0 to 20 years, average 6.7, and of the 23 with no reduction from 2 to 17 years, average 7.8. Average duration of symptoms in the three groups was consecutively 4.6, 6.7 and 6.8 years. During the remainder of this paper results of sympathectomy will be presented separately for each of the three groups.

Effect upon Symptoms of Hypertension. Symptoms attributable to hypertension occurred before sympathectomy in all but two of the 97 surviving patients. With rare exceptions, symptoms when they occurred after operation were much less severe. Incidence of symptoms is recorded in Table II.

It is evident that the number of patients relieved of symptoms is greatest in the group with most reduction of blood pressure and least in the groups with less or no reduction. Exceptions to this observation occur in the column under precordial pain and palpitation. These two symptoms, occurring in 33 and 44 patients, respectively, before operation, were relieved in all but 4 and 3 after-

ward. Since the operation interrupts both nervous pathways conducting pain from the heart and sympathetic cardiac accelerators, elimination of these complaints is expected in all cases. The exceptional persistence in the few might be explained by error inherent in subjective observations. Symptoms listed in Table II are those described during the first several months before operation and those during the last several months preceding this report.

Effect upon Complications of Hypertension. For convenience, incidence of complications of hypertension is presented in Table III. Each of the five major complications will be discussed individually, adding separation into groups according to results on blood pressure.

Cerebral vascular accidents with hemiplegia (Table IIIA) occurred once or oftener before sympathectomy in 19 patients. Sixteen of these patients are now living, seven longer than five years. Of these 16, one now living after eight

TABLE III.—*Complications of Hypertension.*

	Entire Series of 113 Patients Before Sympathectomy	Currently Surviving Series (97 Patients)		
		Preoperative	At 3 Months	Latest Observation (1 or more years)
A. Cerebral accidents with hemiplegia	19	16	0	1
B. Retinopathy				
1. None	73	68	78	44
2. Hemorrhages or exudates	38	29	8	1
3. Papilledema	11	5	1	1
C. Enlargement of heart				
1. None	64	60	43	37
2. Moderate	34	30	38	11
3. Marked	15	7	14	11
D. Abnormalities of electrocardiogram				
1. None	48	45	45	32
2. LAD only	16	13	12	5
3. T Wave and/or ST segment	27	21	21	17
4. Strain	22	18	10	5
E. Diminished renal function	9	5	1	1

years has had three cerebral vascular accidents since sympathectomy but is able to be up and about although activity is restricted. His blood pressure was not significantly reduced by operation. Another patient apparently had a minor cerebral accident one year after sympathectomy but did not develop hemiplegia. Her blood pressure also was not reduced. The remaining 14 patients have not had cerebral vascular accidents since operation. Of the entire group of 16 patients, reduction of blood pressure to normal occurred in five, some reduction in six, and no reduction in five.

Effect upon Hypertensive Retinopathy. Table III B presents the incidence of occurrence of retinal hemorrhages and exudates and of papilledema, grouping all patients together. These complications of hypertension were present before operation in 40 of the 113 patients of the entire series and in 29 of the 97 now living. Of the 31 surviving patients whose blood pressure remains

reduced to normal, 10 had hemorrhages and exudates before operation and three of those also had papilledema. Hemorrhages and exudates disappeared before examinations made three months after operation in eight patients. Two evidenced this complication three months after operation but not during subsequent examinations. Retinopathy has not reappeared in any of these patients. Of the 43 surviving patients whose blood pressure was reduced but not to normal, only eight had hemorrhages and exudates and of these only one had papilledema. This disappeared after operation, although in three patients, retinopathy continued at three months, disappearing later. In no patient observed for longer intervals has it reappeared. Of 23 patients with retinopathy before operation and now living but not having significant reduction of blood pressure, 11 had hemorrhages and exudates and of these three also had papilledema before operation. Afterward, hemorrhages exudates and papilledema persisted in one patient. This patient had been treated by a strict rice diet without effect before and after sympathectomy. When last observed nine months after operation he refused further diet or treatment and has subsequently refused to return for examination. He reports, however, when last contacted four years after operation, that he is well and working regularly. Another patient had exudates but no papilledema one year after sympathectomy. The exudates were described by the ophthalmologist as apparently old. They had disappeared when the patient was examined two and one-half years after operation. A third patient with hemorrhages and exudates present three months after operation has not been back for subsequent observation. With these three possible exceptions, all of the 12 patients in this group having hemorrhages and exudates present before operation and not having reduction of blood pressure afterward have had disappearance of these lesions. Also, they have not to our knowledge had recurrence.

It is evident that hemorrhages and exudates were present before operation least frequently in the group of 43 patients whose blood pressure was reduced but not to normal.

It is of interest that five patients of the 97 had marked reduction of blood pressure during the first week after their last operation and became irrational or developed coma. Three had temporary increase in blood N.P.N. All recovered. During this episode of presumed encephalopathy these five patients had increase of hemorrhages and exudates and mild papilledema, which later disappeared.

The above observations concerning the ophthalmoscopic appearance of the fundus in the entire series of 113 patients are based largely upon the presence or absence of hemorrhages, exudates or papilledema as obtained from patient records of two hospitals. Details of the ophthalmoscopic evaluation in the first 19 patients operated upon at the University of Chicago have been reported by Gans.[19] One of us (B. A.) has examined records of the 94 patients subsequently treated at Duke University. The records of 78 of these patients were sufficiently complete so that results might be evaluated on a basis of appearance of the entire fundus rather than on a basis of occurrence of hemorrhages,

exudates or papilledema. Usually these records included personal observations or fundus photographs. He has evaluated results considering condition of discs, sheathing of vessels, changes in light reflexes and color of vessels, attenuation of arterioles as compared with veins, localized changes in caliber of arterioles or venules, increased tortuosity, accentuation of arterio-venous compression, development of epivascular pigment streaks, appearance of retinal edema, "cotton wool" patches or hard "edema residues" and occurrence or organization of hemorrhage. Rather than attempt grouping according to the conventional Keith-Wagner, Gifford, Gans or Freidenwald classifications, each of which has its definite limitations, this co-author has grouped results of sympathectomy depending upon whether the entire ophthalmoscopic appearance of the fundus revealed hypertensive retinopathy before operation, and whether if present this retinopathy improved, was unchanged or increased following operation. These groups are presented in Table IV and compared with effects of sympathectomy upon blood pressure. Included among the 19 patients with retinopathy unchanged are 15 with minimal abnormalities and four with moderate hypertensive retinopathy. Three of these four had been followed for only three months at the time of latest observation. The fourth had been followed for two years and evidenced increasing vascular change, although exudates present before operation had disappeared. The two patients showing

TABLE IV.—*Effect of Sympathectomy Upon Hypertensive Retinopathy Grouped According to Effect Upon Blood Pressure (78 Patients).*

	Totals	No Retinopathy	Retinopathy Improved	Retinopathy Unchanged	Retinopathy Increased
A. Blood pressure reduced to normal..	24 pts.	6 pts.—25%	14 pts.—58%	4 pts.—17%	0 pts.—0%
B. Blood pressure reduced but not to normal.....	37 pts.	13 pts.—35%	11 pts.—30%	12 pts.—32%	1 pt. —3%
C. Blood pressure unchanged.....	17 pts.	8 pts.—47%	5 pts.—29%	3 pts.—18%	1 pt. —6%
Total.....	78 pts.	27 pts.—35%	30 pts.—38%	19 pts.—24%	2 pts.—3%

increased retinopathy in Table IV are the same two who had hemorrhage or exudate, and in one papilledema (Table IIIB), details of these patients have been described above.

Effect upon Renal Function. Each patient has had conventional examinations of renal function before and at intervals after operation. These always included P. S. P., Mosenthal or Fishberg, blood nonproteins nitrogen or urea nitrogen and often included urea clearance or urea ratio. With few exceptions, pyelograms were obtained before operation. These revealed few abnormalities. Moderate albuminuria was found in some patients, but quantitative albumin studies were not obtained.

Review of work sheets plotting results of tests of each patient before and at intervals after operation has not revealed a definite change or trend. With nine exceptions, renal function was essentially normal before operation. Review of plotted work sheets after operation for the patients with normal renal func-

tion has shown that function has not become impaired during the period of postoperative observation even in those patients who had no reduction of blood pressure and have been followed for several years. Publication of details of these tests does not seem warranted.

The nine patients differing from the others by having evidence of impaired renal function before sympathectomy will be discussed. Four had elevation of blood urea nitrogen. One of these died in uremia after the first stage of the sympathectomy; one died of respiratory arrest shortly after the second stage; two died three years afterward, one of cardiac failure and the other of a cerebral accident. The remaining five patients are now living. Each had reduced renal function as judged by several low phenol-sulphonphthalein clearances or by poor concentration of urine during several Mosenthal tests. Blood nonprotein nitrogen was not elevated. Three were treated medically by sedation and a rice diet during several weeks in the hospital before sympathectomy. Diminished renal function as judged by these tests persisted in only one after operation.

Effect upon Size of the Heart. As indicated in Table III C, 49 of the original 113 patients had enlargement of the heart, moderate or marked as arbitrarily judged by review of chest roentgenograms taken at six feet or in a few instances by fluoroscopy. Detailed measurements of the cardiac shadow in films and adjustment according to weight and height permitted calculation of percentages of deviation from average normal heart size in 86 patients. Using such accurate measurements when possible and other information when not possible, all patients were grouped according to whether hearts were not enlarged or were moderately or markedly enlarged. Patients grouped in Table III C as having moderately enlarged hearts had a percentage deviation from normal of plus 11 to 20 per cent. Those grouped as having markedly enlarged hearts had a deviation of plus 20 per cent or more. It is evident from Table III that of the fifteen patients having marked enlargement before operation only seven are now living.

Of the 97 patients currently surviving, 30 had moderate and seven marked enlargement before sympathectomy. It is evident (Table III C) that three months after operation the number with marked enlargement of the heart increased, occurring in 14 of 95 patients. At the time of the last observation, a year or more after operation, the number with marked enlargement remained relatively increased, occurring in 11 of 59 patients examined. The number with moderate enlargement also increased at three months but then decreased after one or more years. Explanation of this relatively poor effect of sympathectomy does not develop when results are separated into three groups according to effect upon blood pressure.

Among 31 patients now surviving with blood pressure at near normal values, cardiac enlargement was moderate in seven and marked in none before operation. Of 30 examined at three months, eight had moderate enlargement and two marked enlargement. Of 21 examined subsequently, only three had

moderate and none marked enlargement. Of 43 patients with blood pressure reduced, 16 had moderate and two marked enlargement before operation. At three months 42 patients were examined and of these 24 had moderate and three marked enlargement. Subsequently, however, of 23 examined, six had moderate and three marked enlargement. Among 23 patients without significant reduction of blood pressure, seven had moderate and five marked enlargement before operation. At three months, six of 23 patients examined had moderate and nine marked enlargement. At a year or more, 13 patients were examined and of these two had moderate and eight marked enlargement.

It is evident that for some unexplained reason the incidence of patients having either moderate or marked enlargement of heart size increased during examinations made three months after operation. It is also evident that incidence tended to decrease in later observations. The decrease, however, was definite only among patients with reduction of blood pressure to near normal. Decrease of incidence of moderate enlargement of the heart occurred among those patients with reduction of blood pressure but not to normal. Incidence of marked enlargement increased, however, and the total percentage of those with enlargement, therefore, remained little changed. Among patients with no reduction of blood pressure incidence of enlargement increased.

Effect upon the Electrocardiogram. The most significant effect evident in electrocardiograms obtained before and at intervals after sympathectomy is a constant decrease of heart rate following operation. This persisted throughout the period of postoperative observation. As illustrated in Table III, a comparison preoperatively and at three months of incidence of the patients with normal electrocardiograms (D 1), those with left axis deviation only (D 2), those with this plus significant T wave and/or ST segment abnormalities (D 3) and those with definite strain patterns (D 4) reveals a marked similarity before and after operation in each of the first three categories. Only in incidence of strain pattern (D 4) was there a definite decrease. At one year or more there was a moderate decrease of incidence of left axis deviation and of strain pattern but a definite increase of the proportion of patients exhibiting T wave and/or ST segment abnormalities. Presentation of these varying effects is somewhat aided by separation of results into three groups according to effect of operation upon blood pressure.

Among 31 patients now surviving with blood pressure at near normal values, electrocardiograms were normal before operation in 20, demonstrated L. A. D. in four, T wave changes in three and strain pattern in four. At three months, distribution was essentially the same. Of 20 patients followed for a year or more, 13 had normal electrocardiograms, one had L. A. D., four demonstrated T wave changes and two showed strain patterns. Incidence of abnormalities among patients surviving with reduction of blood pressure but not to normal was, before operation, 23 normal, three L. A. D., ten T wave abnormality and seven strain pattern. At three months and at one or more years, incidence of abnormal electrocardiograms was essentially the same, only two

improving by exhibiting change from strain pattern to T wave abnormality. Of 23 patients with no reduction of blood pressure, electrocardiograms were normal before operation in only two, L. A. D. was present in six, T wave abnormalities in eight and strain pattern in seven. At three months, five of 20 examined had normal electrocardiograms, five had left axis deviation, six had T wave abnormalities and three showed strain patterns. Of 15 patients followed for one year or more, five had normal electrocardiograms, two showed L. A. D., six T wave changes and two strain patterns.

In general, the above study of results of sympathectomy as judged by electrocardiogram has demonstrated little effect. Decrease in the incidence of strain pattern and other abnormalities apparent in some groups might be explained by failure of a few patients exhibiting these abnormalities to return for their examinations after a year.

Effect of Subsequent Pregnancy. Four patients became pregnant after sympathectomy. One patient, whose blood pressure had been normal during six years, delivered normally at term. Blood pressure, normal before and after delivery, rose for a few hours during labor to 180/110 but subsequently has remained normal. Another patient, whose blood pressure had been normal for one year following sympathectomy, developed moderate elevation of pressure during her nine months, the highest reading being 220/140 at term. Following delivery her pressure returned to normal gradually during the next year and a half. The third patient with reduction of blood pressure to normal became pregnant during the first months after sympathectomy. Blood pressure remained normal during the first seven months of pregnancy and then rose, the hospital average at the time of delivery being 196/134. Pressures then returned to normal. This patient again became pregnant, delivering her second child a year and a half later. Hypertension reappeared during the last two months of pregnancy and remained at high levels following delivery.* The fourth patient also had reduction of blood pressure to normal for 14 months. She then became pregnant, but refused prenatal care. She is the patient (described above under survival statistics) who died of a toxemia of pregnancy with blood pressures as high as 248/180.

DISCUSSION

It is now well-established that splanchnicectomy may be an adjunct to the treatment of hypertension in certain patients. Many observers, however, feel that results following this operation are frequently poor or temporary. Results of extending sympathectomy to include the stellate and upper thoracic ganglia as well as the nerves usually removed during modern operations for splanchnicectomy have been presented in some detail so that the reader may judge whether the frequency of poor or temporary results has been decreased by this more complete sympathectomy. It is our impression, based upon experiences with splanchnicectomy in another series of patients, that this has happened.

The observations presented above apparently indicate that, with few

* Since preparation of the paper, this patient died of a cerebral vascular accident.

exceptions, progression of the hypertensive disease process has been retarded or in some patients even arrested. Also, reduction of blood pressure, relief of symptoms, prevention of recurrence of complications and elimination of hypertensive retinopathy has occurred in most patients. The only observations that have not indicated much improvement are those based upon heart size and electrocardiograms. Survival statistics seem to indicate that, considering the type of patients selected for operation, life expectancy has been increased. It must be emphasized, however, that these patients represent a selected group and that a suitable control series has not been possible. Selection has included patients under 50 years of age who do not have elevation of blood nonprotein nitrogen, hypertensive encephalopathy with increased intraspinal fluid pressure or infarction of heart muscle and who exhibit reasonably adequate emotional stability. Selection has excluded patients with mild or nonprogressive types of hypertension.

Of the various possible etiologic factors presented in the introduction of this paper, only one, the neurogenic, would explain entirely the results obtained and the apparent improvement of results over those observed or described after splanchnicectomy alone. This, unfortunately, cannot be interpreted as proving that these patients had neurogenic mechanisms as the initiating and perpetuating factor of their hypertension. Sympathectomy may have nonspecific effects resulting from denervation of the vascular bed or the viscera which might indirectly influence other hypertensive mechanisms.

Special tests of the circulation were obtained in some of the patients described above and will be discussed. They have shown that following sympathectomy total blood volume, blood viscosity and renal blood flow were not significantly altered. Details of these tests will be reported by W. Adams, A. Alving and others. Cardiac output values, determined in nine patients by W. Adams using a modification of the acetylene method, ran slightly lower after operation than before. He suggests that decrease of cardiac output approximately parallels reduction of heart rate. Cardiac output values, determined by J. Hickam employing the Fick principle and using the cardiac catheterization technic, revealed little deviation or slight reduction below normal with patients in the supine position. The moderate changes of cardiac output observed by Adams and Hickam had no relation to reduction or failure of reduction of blood pressure following sympathectomy. Hickam also observed that as blood pressure was reduced by postural changes during tilting, further reduction of cardiac output occurred. This reduction did not exceed that expected during tilting of normal patients. Also he observed that moderate exercise in the supine position in these sympathectomized patients resulted in an increase of cardiac output similar to that occurring in normal patients. Since blood volume and blood viscosity were not definitely changed in the sympathectomized patients tested and since cardiac output was little reduced, one must assume by exclusion that the total peripheral resistance was decreased following operation in those patients having reduction of blood pressure.

Results of the cold pressor test (Hines[20]), performed on all patients before and after sympathectomy are not reported in detail since they evidently contributed little or no information relative to advisability of operation or result. Immersion of one hand in ice water usually produced prompt increase of blood pressure before sympathectomy and also afterward, even though the operation had effected denervation of thoracic and abdominal viscera together with loss of sweating of as much as 54 to 98 per cent of the body surface area.

Similarly, rest and Sodium Amytal tests[12] failed to predict the effect of sympathectomy, and results will be discussed without presenting details. Analysis of individual graphs of blood pressure readings obtained hourly during a 24-hour study period revealed that the lowest single diastolic reading reached during preoperative tests was less than the average recumbent blood pressure of the patient during the first several weeks after sympathectomy in half the number and higher in half. If the general low level during the preoperative test rather than the lowest single diastolic reading is compared with the average recumbent diastolic blood pressure during a week in the hospital one or more years after sympathectomy, then the test level is lower than the late postsympathectomy level in a little less than half the number of patients and higher in a little more than half. Analysis of these data evidently indicates that results of the Sodium Amytal tests are not significant.

The basal metabolic rate was determined in 23 patients before and after sympathectomy. Postoperative determinations were made at intervals up to four years after operation. With one exception there was a slight decrease of basal metabolic rate both shortly after operation and during tests obtained up to four years later. Since the average B. M. R. before operation was plus 4, the average several weeks afterward minus 4 and the average one to four years later only minus 11, the changes were not considered significant. Most patients gained in weight.

Blood pressure readings presented in this paper have been taken in the supine position after rest. With exercise, and particularly with erect posture, additional reduction of blood pressure occurs. This is true in all patients including those whose blood pressure in the supine position was not significantly reduced by operation. It is of interest that although before operation blood pressure increased immediately after exercise in those patients tested, afterward there was a decrease, frequently rather large, in all tested. Postural lowering of blood pressure as judged by systolic levels has persisted in all patients. As judged by diastolic blood pressure, it has persisted in most, only a few, several years after sympathectomy, having a slight increase of diastolic pressure while standing. Bradycardia effected by sympathectomy persists in the upright position. Even after exercise, such increase of heart rate as occurs seldom approaches the normal or preoperative resting rate of 70 to 80 beats per minute.

Experiences with four patients pregnant at some time after sympathectomy have indicated that hypertension may recur during this condition. Although

the new elevation of blood pressure receded following delivery in two patients, elevation of blood pressure persisted at high levels in another two, causing complications leading to death. It therefore does not seem advisable that pregnancy be recommended following sympathectomy for hypertension.

One patient treated four years preceding our latest follow-up report had his sympathectomy because of polycythemia vera and hypertension. Detailed studies of his blood were reported by Schafer.[21] They indicated definite decrease of volume and number of red blood cells following sympathectomy. Although he had been treated by withdrawing blood at frequent intervals during two years preceding operation, this has not been necessary afterward, and the patient reported after four years that he remained well. Another similar result in a second patient with polycythemia has led to the impression that sympathectomy may be recommended for some patients with hypertension and polycythemia.

Finally, it should be emphasized that near total sympathectomies are associated with certain disabilities or inconveniences. Some of these complications persist only during the first several months after operation. Of these, the most serious has been pain, which occurs in all patients and is intense in many. It has lasted in occasional patients as long as a year. Postural lowering of blood pressure occurs and usually produces disability during the first several months after operation. Symptoms of dizziness when standing rarely persist a year. Following this period of time, postural lowering of blood pressure persists but is not associated with disability. Other complications unfortunately persist, although they are somewhat less troublesome after a year or two. One of these is excessive sweating occurring in areas of regeneration or in areas not denervated. This produces inconvenience by moistening clothing, particularly during hot weather. Another persistent symptom is partial obstruction of nasal airways caused by swelling of the mucous membranes. This occurs in many patients but has been sufficiently troublesome to warrant injection of sclerosing agents in only a few. Although the above inconveniences or disabilities have been moderately annoying to some patients, they have not been sufficiently serious to discourage our belief that near total sympathectomy is indicated for many disabled by hypertension.

CONCLUSION

Total thoracic and partial to total lumbar sympathectomy, splanchnicectomy and celiac ganglionectomy in a substantial majority of a series of 113 hypertensive patients has apparently retarded and in some even arrested the hypertensive disease process.

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AN EVALUATION OF THE TREATMENT OF ESSENTIAL HYPERTENSION BY SYMPATHECTOMY*

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SYMPATHECTOMY has been done in this country for hypertension since 1933 and yet there is still lack of agreement as to its usefulness in this disease. In 1942, Grimson[1] estimated that at least 3,000 patients had been treated in this way and by now this number must have more than doubled. Despite this large experience, varied opinions are still prevalent regarding the results obtained. It is the purpose of this communication to point out some of the reasons for the existing confusion and to review our own experience with 105 patients with essential hypertension treated by sympathectomy. Nephrectomy and removal of pheochromocytomas for hypertension will not be discussed.

It has been my contention that the final decision regarding the value of sympathectomy for hypertension will depend upon whether two purposes are accomplished by the operation, that is, relief of symptoms and prolongation of life. If a patient lives comfortably to a ripe old age, would it matter if the blood pressure were maintained at high, abnormal levels? Hence, a precise knowledge of these two factors would be enough for evaluation of the procedure. Obviously, one has only to compare a series of patients who have been operated on with a series of patients who have been treated by nonsurgical measures. Such comparisons lead to one conclusion at least, namely, that the operation brings about relief of symptoms in approximately 80 to 85 per cent of the cases. Therefore, this important question can be answered with assurance, but in regard to prolongation of life, there is much less agreement. The reasons for this lie in the fact that a number of different operations are still being done for hypertension, and classification of the patients is difficult because of our ignorance concerning the fundamental factors in the disease.

At present splanchnicectomy is being performed both above[2] and below[3] the diaphragm. Ablation of the splanchnics and a portion of the sympathetic chain above and below the diaphragm at the same time, as advocated by Smithwick,[4] is perhaps the most widely used procedure; also popular at several large clinics is a more extensive excision, first advised by Grimson.[5] Although the advocates of each operation believe in the superiority of the procedure of their preference, it is my belief that probably all operations accomplish the one essential—denervation of the adrenals. Widespread denervation increases the postural hypotension; however, there is no proof that this manifestation indicates benefit to the patient. This sequel to operation usually disappears within one year; yet three of our patients still have a small diminution in pressure in the erect position after three years. Some advocates of wide excision of the

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sympathetics maintain that the late elevation of blood pressure always is due to regeneration of these nerves. Although this may occur, the renewed high levels are probably more often a manifestation of the progressive changes in the vascular system which are taking place. Certainly little proof that regeneration is the cause has accumulated.

It has long been known that some hypertensive patients live comfortably with the disease for many years. Perera[6] recently pointed out, after following a large group of patients for years, that there is no constant correlation between a persistently high blood pressure and those complications which are usually regarded as following in its wake. Our ignorance of the fundamental pathologic process makes exact classification difficult; yet this is necessary if we are to predict the course of the disease in the individual patient. In order to do this, we must know the type of hypertension being operated upon and what can be expected if operation is withheld. At present, we must content ourselves with generalizations.

It is recognized that the prognosis in malignant hypertension is poor, regardless of treatment, and indeed, there are those who maintain that sympathectomy has little effect in prolonging life when this condition prevails.[7] On the other hand, other surgeons claim results which, though not brilliant, are considered worthwhile.[8] The same difficulty with classification is encountered when milder, less progressive disease is present; in fact, the future of these patients is less predictable than it is in the more severe types. The obvious need for a better selection of patients for surgical treatment has initiated investigations regarding blood pressure characteristics,[9] effects of caudal anesthesia,[10] spinal anesthesia and development of clinical rules.[11] We utilize high spinal anesthesia and the Sodium Amytal test routinely but have not been greatly impressed with their prognostic value.

The difficulties in comparing the results obtained in analogous series, one treated surgically and the other medically, are illustrated by reports of Keith, Wagener and Barker,[12] Peet[2, 8] and Flaxman.[13] The latter, who studied 244 patients fulfilling Peet's requirements for operation, noted that there were as many of his medically treated patients alive at the end of five years as there were in Peet's series of patients who had splanchnicectomy. Again, Peet reported 21 per cent of 143 patients with malignant hypertension treated by splanchnic resection alive at the end of five years, whereas in the Wagener-Keith series only one of 146 patients was living after five years of medical treatment. Some of these discrepancies probably depend on the variations in classification of the disease currently in use. Hence, it would be a distinct step in advance if a responsible professional body formulated an acceptable classification of hypertension which would be exact enough to permit comparison of patients treated by various methods.

Our own experience consists of 105 patients with hypertension who had bilateral thoracolumbar sympathectomy and splanchnicectomy prior to October, 1947 (Table I). The sympathetic chain and splanchnics were removed from the level of the seventh thoracic vertebra down to the third lumbar ganglion.

Sixteen other patients were excluded because either a nephrectomy also was performed or only unilateral sympathectomy was done. In each instance a careful study was made by our medical department and no patient was operated on who did not have symptoms and unmistakable evidence of progressive hypertensive disease. The youngest patient was 21 years of age and only three were 50 years or more. Heart failure and urea clearance of less than 50 per cent were considered contraindications to operation. Several patients had had cerebral vascular accidents. In reality, selection is based largely on the extent of the organic disease and resulting damage to the cardiovascular system and kidneys. Hence, the rules should not be too rigid except beyond certain limits. This is illustrated by our oldest patient, a man of 59 years, who had only moderate organic changes. Even though he had severe hypertension and incapacitating symptoms, the results of sympathectomy were excellent.

TABLE I.—*Classification of 105 Cases of Essential Hypertension Treated by Sympathectomy*

	Cases	Per Cent
Group I	8	7.6
Group II	63	60.0
Group III	34	32.4
Total	105	100.0

The cases were classified into three groups. Group I consisted of young persons with somewhat variable hypertension, little cardiovascular disease, normal renal function and minimal retinal changes and symptoms. Group II usually included older persons with progressive hypertension, definite cardiovascular disease, often some reduction in renal function and moderate to

TABLE II.—*Blood Pressure Response of Followed Patients in Group I*
Average Preoperative Blood Pressure 176/112

	Blood Pressure in Mm./Hg. Years Postoperative		
Case	1	2	3
1	155–100	180–100	170–120
2	190–110	190–110	
3	140–90	160–110	
4	140–94	150–90	150–90
5	150–90	150–100	
6	160–105	140–90	

severe retinal changes and symptoms. In Group III the patients had a fixed diastolic pressure above 140 millimeters of mercury, cardiovascular disease, reduction in renal function, severe retinal changes and acute symptoms.

There were four postoperative deaths in the entire series. Data on the patients' course after operation were obtained by follow-up examinations which usually included an electrocardiogram, urea clearance test and examination of the optic fundus.

It is believed the principal interests of this study are the results obtained at the end of one year. This period is admittedly too short for a comprehensive evaluation, but it is generally conceded that the results become less favorable

with the passage of time and hence the optimum should be reached about one year after operation. By establishing such a yardstick, the information thus obtained might profitably be compared with data embracing longer periods.

There were eight patients (7.6 per cent) in Group I, two of whom could not be traced. As shown in Table II, in only two patients could the blood pressure be considered normal one year after operation. Two other patients obtained little reduction in blood pressure. At the end of two years, again only two had pressures that could be considered normal. There were no deaths in this group, and all patients obtained satisfactory symptomatic relief.

TABLE III.—*Followed Patients in Group II*

Follow-up	1 yr.	2 yr.	3 yr.
Living	40	18	8
Dead	3*	0	0
Total	43	18	8
Per cent of patients followed who are living	93	85	72

* 2 were postoperative deaths.

Group II contained 63 patients, only 40 of whom were followed for one year (Table III). There were two postoperative deaths and only one other death during the year. We are not aware of any deaths in the second and third years, but the number of patients followed becomes smaller and more time will be required to evaluate this group over a longer span. In only 40 per cent of the patients was the blood pressure response good at the end of the

TABLE IV.—*Results in 40 Patients in Group II Followed One Year*

	Cases	Per Cent
Blood pressure response		
Good (almost normal or normal)	16	40
Fair (reduction but levels definitely abnormal)	12	30
Poor (little significant reduction)	12	30
Definite improvement in retinal changes	12	30
Definite improvement in cardiac status	14	35

first year, but most of these still had manometric readings which must be considered abnormal (Table IV). Twelve (30 per cent) had a definite reduction in blood pressure but the levels remained abnormally high. Another 12 (30 per cent) were little improved from this standpoint. Of the 40 patients, 12 exhibited definite improvement in the retinal changes and 14 showed unmistakable improvement in the cardiac status.

There were 34 patients (32 per cent) having malignant hypertension (Group III), of whom 28 have been followed for one year (Table V). Six of these died, two of them postoperatively. Although 78 per cent of the patients followed were alive at the end of one year, this figure was reduced to 23 per cent at the end of three years. Of the 22 alive at the end of the first year, only two had near normal blood pressures, but seven had obtained a fair response (Table VI). Six of the 22 showed improvement in retinal changes.

The symptoms accompanying hypertension do not always bear a relationship to the height of the blood pressure. This is true both before and after operation. In our patients, symptoms were relieved in over 80 per cent of the patients even though at times there was not a concomitant fall in blood pressure. Many observers have described improvement in renal function following sympathectomy; thus, Peet[2] claimed that "45 per cent of the patients with abnormal urea clearance have returned to normal and 44 per cent with impaired water concentration have marked improvement." Similar improvement in our patients was not evident.

Reports now available reveal numerous discrepancies when compared with our experience. Again, Peet[2] stated that 20.3 per cent of his living patients

TABLE V.—*Followed Patients in Group III*

Follow-up	1 yr.	2 yr.	3 yr.
Living	22	9	3
Dead	6*	3	1
Total	28	12	4
Per cent of patients followed who are living	78	50	23

* 2 were postoperative deaths.

have maintained normal blood pressures following splanchnicectomy for five to twelve years, whereas Smithwick[9] noted improvement in blood pressure in 66 per cent of a large series followed for one to five years. A comparison of these results with our experience makes it clear that our results at the end of one year are less satisfactory even though the operation was adequate according to the criteria of both Peet and Smithwick. Numerous other reports could be cited to illustrate the diverse interpretations of the results following sympathectomy.

TABLE VI.—*Results in 22 Patients in Group III Followed One Year*

	Cases
Blood pressure response	
Good	2
Fair	7
Poor	13
Definite improvement in retinal changes	6

SUMMARY

A more exact and uniform classification for hypertension obviously is needed to enable a better selection of patients as well as to allow a better interpretation of the results. We have been interested particularly in the results after one year because it is believed that these represent the optimum and therefore, they can be used as criteria for measuring remote end results.

The present study confirms the ability of sympathectomy to relieve hypertensive symptoms in more than 80 per cent of well-selected patients. Our experience has not provided a definite answer as to whether life is prolonged.

The operation is probably justifiable for relief of symptoms alone, although it is our impression that many of the patients having sympathectomy live longer than they would have if operation had not been performed.

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DISCUSSION.—DR. WINCHELL MCK. CRAIG, Rochester, Minn.: Doctor Grimson and Doctor Penick have brought us up to date with regard to the surgical treatment of hypertension, which I attempted to do before this group two years ago. Although Doctor Grimson presented an excellent argument for total sympathectomy, I still wonder whether this is not a pretty radical procedure for some of the patients suffering from hypertension and whether we should not reserve it for a special group.

Some of us who have been performing surgical operations for hypertension for a period of years have had a tendency to think of progressive hypertension very much as we do other types of malignancy; that is, that any patient who has hypertension which fails to respond to medical measures and progresses should have surgery. However, if our follow-up studies have been of any value, they indicate that some patients who have the more advanced hypertension have irreversible changes which cannot be altered by surgery. Although it is true that in some cases in the early stages remissions may occur, in the group of cases which we have followed, in which hypertension Groups II or III has developed in a short period, the hypertension can be controlled by surgical procedures. It is controlled from the standpoint of blood pressure and appearances of the fundi, as well as alleviation of symptoms.

So many factors are present in the etiology of progressive hypertension that we must recognize the disease in its early stages if we expect to approximate the five-year cures obtained by the surgical treatment of malignant lesions. We cannot overlook the fact that Ayman pointed out a definite hereditary factor, which has been developed by Hines and Brown, and that entire families with a bad heredity have hypertension in spite

of all types of treatment. There is no question but that surgical procedures in this group have changed the prognosis in a certain number of cases and these results have been obtained with a less radical procedure than is outlined by Doctor Grimson.

I think we are all interested in this problem from the standpoint of a minimal amount of surgery for a maximal amount of benefit. If total sympathectomy is indicated in a certain group of cases and it can be proved that these patients are comfortable, are able to return to work and enjoy life in general, then it can be endorsed. If, on the other hand, some of the patients are not comfortable or able to return to gainful occupations, even though the blood pressure is lowered, the question will remain in some of our minds as to whether a less radical procedure would not have served the purpose.

The physiologic effect of the removal of all or a portion of the sympathetic nervous system needs to be evaluated, not only from the standpoint of the effect on the blood pressure but the over-all picture of the disease, and it is such reports as we have heard today which help us to evaluate the treatment of hypertension by surgery on the sympathetic nervous system.

Dr. Frank H. Lahey, Boston: I always feel embarrassed in discussing papers on hypertension because I do not know anything about it. As I said when I discussed Doctor Craig's paper last year, it does seem that this is so important that all data available should be presented in order that we may have as much information as possible upon which to make decisions as to the value of the principles involved in the surgical treatment of hypertension, and in evaluating methods. Doctor Poppen presented me with figures from the Clinic in which it has been possible to compare the results in 100 cases, as I reported two years ago for him, report on which was published by Doctor Poppen and Doctor Lemmon in the Journal of the American Medical Association. In these cases the resections were from the tenth thoracic through the second lumbar, and from the sixth thoracic to the second lumbar. This group can now be compared with 275 cases in which all the resections were from the fourth thoracic through the second and third lumbar. These cases have been followed by Doctor Evans and Doctor Bartels in the medical department, and it will be of interest, particularly in the light of these two papers, to present the comparison of some of the results in the latter group of cases.

We have also been interested, as we have watched these cases, to observe that the effects on patients with Group III hypertension (Keith-Wegener formula) have been striking in the degree of improvement in the more extensive resections, as compared with less radical ones. In the earlier group there was only 4 per cent definite improvement, as compared with 44 per cent in the latter group. In Groups I and II it has been of interest to compare the groups. While these figures are only approximate, I have always remembered the report of the first group in terms of satisfactory, fair, and unsatisfactory.

In the first group, satisfactory results were obtained in roughly 50 per cent; fair results in 25 per cent, and unsatisfactory results in 25 per cent. The figures in the latter group have changed to 70 per cent satisfactory, 20 per cent fair, and only 10 per cent unsatisfactory. Some of the other results have also been interesting. In 15 patients with angina, 60 per cent were relieved. On the other hand, none of these had serious coronary disease.

There was improvement in 42 per cent of 50 patients who had abnormal electrocardiograms. Renal function tests were improved in 58 per cent of 55 patients who had had one or more impaired tests before operation. Retinal vascular change improved in 66 per cent of 170 patients. This should settle the question as to whether the more radical procedure should be done. The mortality in the first group was 0.5 per cent and in the second group is still 0.5 per cent. This is interesting because all, or practically all, have been done by one surgeon (J. L. P.). We should be loath to consider this type of operation, with its prolonged, uncomfortable convalescence, as a prophylactic operation for benign hypertension, but urge it on patients under the age of 50, with spastic, exudative and hemorrhagic retinal arterial changes, moderate cardiac damage and signs of early nephrosclerosis.

I have often looked over Doctor Poppen's shoulder and have seen regeneration around the silver clips placed on the sympathetic nerves in previous operations in the hope that they might retard the progress or rate of growth. It is true that the splanchnic usually originates at the sixth level, and may in the fourth, and he feels because of this, that with removal at the fourth there is less likelihood of regeneration of the splanchnic branches. I present these figures so that they may be available to everyone.

DR. JOHN FALLON, Worcester, Mass.: During the adolescence of any operation, especially one so important as this, it seems advisable to accumulate quickly the scattered reports of complications, tragedies and other unexpected results. There is nothing I can do to express my gratitude to your Association for your hospitality better than to tell you about a patient whom I would rather forget.

Some years ago we had a patient who, following the unexpectedly high climb of a spinal anesthetic had minor but permanent effects of cerebral anoxia. That made us conscious of the complications which might occur from hypotension during the operation for hypertension. Before starting to do sympathectomies we tried various methods, reported and otherwise, of controlling temporary hypotension, including a pressurized suit such as is used by aviators to prevent blackout. In spite of this awareness we had a total paraplegia at the eleventh dorsal in a patient aged 50 with severe malignant hypertension. The operation was a Smithwick, the anesthesia nitrous oxide-ether, and she awoke from the anesthesia with a paraplegia which still persists. The spinal fluid and its pressure were normal. Was it an accident; was it a surgical error? If an accident, how likely is it to occur with this operation? We think it likely to be from temporary ischemia or thrombosis of vessels, especially the anterior spinal artery. During operation this patient, whose vascular system was accustomed to a pressure of 300, had a pressure of less than 60 for several minutes despite the inflow of saline and blood, started before operation. She was not subjected to any of the experimental methods we have used to prevent hypotension, so these cannot be blamed.

DR. KEITH S. GRIMSON, Durham, N. C. (closing): The interest of the discussors is appreciated. Several have mentioned relationship of causes of hypertension to results of sympathectomy. We have postulated neurogenic mechanisms as an important initiating and perpetuating cause of clinical hypertension. Results of near total sympathectomy as presented would seem to confirm this hypothesis at least for many of the patients treated. There are, as described in the manuscript, several other important causes of hypertension that might not respond to surgery. Persistence of these other etiologic factors might account for some of our failures.

Experiences with splanchnicectomy performed in another series have been less satisfactory than those reported for near total sympathectomy. These results agree with those for splanchnicectomy reported by Doctor Penick and we agree with his statement that benefits obtained by this operation are often equivocal. Doctor Craig has well stated that the problem of hypertension is large and that surgery is only one approach. Sympathectomies are uncomfortable and temporarily disabling. Also they are performed with some risk of operative mortality. Even though mortality rates can be reduced and the proportion of good results increased by operating upon patients with milder forms of the disease as he suggested, we cannot agree with this practice. It is our opinion that surgery is not indicated for patients with mild hypertension and also that, by using near total sympathectomy, one may aid patients with more serious forms of the disease at an only slightly increased risk.

Doctor Lahey's excellent report of results obtained by Doctor Poppen is very interesting. His statistics would seem to indicate that extension of splanchnicectomy upward to include denervation of thoracic somatic segmental distribution as high as that supplied by the fourth thoracic ganglia has improved results of splanchnicectomy. From the physiologic point of view this seems improbable. There are two explanations of improvement of results which should be evaluated. One is that each time the technic of splanch-

nicectomy is changed, results early and perhaps temporary must be contrasted with the later results of the earlier series. The second explanation is that most surgeons using splanchnicectomy have with increasing experience tended to limit their selections of patients to milder forms of the disease. Doctor Poppen's excellent studies when reported in detail will undoubtedly evaluate these factors. In the meanwhile, extension of his operation to include the remaining upper three ganglia and stellate would add thoracic and cerebral visceral denervation and interruption of adrenergic pathways to head, neck, shoulders, arms, and upper chest. This would permit comparison of results of their then near total sympathectomy with results of their now extensive splanchnicectomy. Such a comparison would be welcomed.

We are in entire agreement with Doctor Waldron that trial of different operations is good. Up to the present time each surgeon extending sympathectomy has continued using the more extensive denervation, and no one to my knowledge has reverted to the earlier more limited procedures.

Dr. Fallon has described an instructive and important danger; that of hypotension during operations upon patients with cardiovascular disease. Occurrence of shock during operation may cause irreparable damage to the central nervous system or the heart. Marked reduction of blood pressure can be avoided by routinely using blood transfusions, intravenous fluids, and peripherally acting vasoconstrictors during operation. Also, it is our opinion that use of the transthoracic approach rather than the posterior dissections through muscles of the back, markedly decreases the operative time and reduces trauma and blood loss, thus diminishing danger of surgical shock. The transthoracic approach decreases magnitude of operation and at the same time permits better visualization of the sympathetic chain, and more extensive removal.

PRESACRAL ENTEROGENOUS CYST*

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This paper presents a case of enterogenous cyst located in the presacral area. It is also our desire to present each case of histologically proved enterogenous cyst that has been reported in the literature as occurring below the peritoneal reflexion.

Enterogenous cyst is a term applied to congenital cysts which have their origin from some portion of the digestive tube. The literature is filled with reports of these cysts arising from the stomach and from the small and large bowel, but reports of cases involving the rectum are scant. It is our desire to report only the cases that have arisen ventral to the sacrum and below the peritoneal reflexion.

Ten reported cases that carry histologic proof of enteric origin have been found in the literature. To this number we wish to add the following case report.

CASE REPORT

Mrs. L. L., a white woman age 33, consulted us on May 12, 1948, complaining of indigestion of two years' duration. Her history was suggestive of duodenal ulcer. There was no complaint of any rectal difficulty, but in the course of physical examination a smooth, fluctuant tumor was felt posterior to the rectum and in close approximation to the coccyx. The tumor was slightly movable in all directions and was not excessively tender to pressure. The finger, on rectal examination, could reach the dome of the tumor and its size was estimated to be that of an English walnut. Proctoscopic examination revealed only a smooth rectal wall over the tumor. Air contrast roentgen-ray studies of the rectal ampulla showed no tendency for the tumor to protrude into the posterior rectal wall. Roentgen-ray studies of the sacrum revealed an indefinite soft tissue mass just ventral to the coccyx. The tip of the coccyx was bent forward at a right angle from the lower sacral segment. All laboratory examinations fell within normal limits except that stool examinations were positive for occult blood. Roentgenographic visualization of a duodenal ulcer confirmed a typical ulcer history.

She was placed on medical management for the ulcer, and the systemic response was rapid. During the course of her early ulcer management we had time to become familiar with lesions occurring in the presacral area by study of the literature. A case report by McLanahan and Stone[3] made the tentative diagnosis of enterogenous cyst tenable in our case. The patient readily agreed to the removal of the tumor. Because of the close approximation of the tumor to the posterior rectal wall, it was thought wise to administer sulfasuxadine for ten days prior to surgery.

OPERATION

On June 8, 1948, the tumor was removed through a posterior three inch midline incision from the anus to the coccyx. It was necessary to remove the distal segments of the coccyx to uncover the tumor in its entirety. With a finger against the tumor from the inside of the rectum, the mass was dissected free from its attachment to the posterior rectal wall, and after enucleation, the gloved finger could be seen clearly through the bowel mucosa. No tissue being available for obliteration of the space occupied by the

* Read before the Southern Surgical Association, White Sulphur Springs, W. Va., December 9, 1948.

tumor, the wound was dusted with sulfathiazole and a soft rubber drain inserted beneath the skin. Drainage persisted for ten days, when healing became complete.

PATHOLOGIC DIAGNOSIS

Gross Examination. The specimen consisted of a well-encapsulated, thin-walled cyst measuring 2½ x 1½ centimeters. Cut section revealed the cyst to be filled with thick, mucoid material. The wall was lined with a pink, soft, mucosalike tissue and measured 0.2 centimeters in thickness.

Microscopic Examination. Sections were made from many different areas of the cyst, and were stained with hematoxylin-eosin, azocarmin and mucicarmin, respectively.

FIG. 1.—Gross appearance of the enterogenous cyst.

Sections stained with hematoxylin-eosin showed the cyst wall as built of the following layers: an epithelial layer and a sub-epithelial layer, loosely arranged, containing small vessels, cell formations like plasma cells, large mononuclear lymphocytes and wandering cells. This layer was followed by two coats of tissue consisting mainly of smooth muscle layers. In addition to these muscle layers, collagenous and reticular connective tissue were present, as indicated by azocarmin stain.

The outermost layers of the cyst were indistinct, and peritoneum could not be demonstrated. Between the outer and inner layers, we found bundles of nerves and in one instance a collection of ganglion cells. By this description the tissue is that of intestinal wall if the epithelium presents the characteristic features of bowel mucosa. Under normal conditions, the mucous membrane of the intestine consists of high columnar, mucus-secreting cells arranged to a certain pattern. In our case, the covering epithelium also consisted of several layers of squamous or transitional epithelium. The cells in the squamous area were in several layers, the lower one more columnar in type, while the uppermost layer showed a more balloonlike cytoplasm. There were areas where this cell layer did not

consist of squamous epithelium but of mucus-producing columnar epithelium, proved by the use of mucicarmin stain.

Stains with iron hematoxylin and with mucicarmin prove furthermore the presence of a cuticulum. Cells of this type are met with in the whole intestinal tract from the cardia to the anus.

Practically all layers characteristic for intestine were demonstrable, namely, mucus-producing columnar epithelium, smooth muscle layers with vessels and nerves. The presence of squamous epithelium is attributed to the effect of metaplasia.

Diagnosis. Enterogenous cyst.

TABLE I.

Author	Year	Author's Diagnosis	Pathologic Diagnosis	Age and Sex	Symptoms	Treatment
Middledorpf	1885	Cyst of postanal gut origin	Small loop of vestigial intestine	1 yr., F		Posterior excision by Kraske
Ballantyne	1932	Cyst of postanal gut origin small area of adenocarcinoma	Cyst of intestinal origin with early adenocarcinoma	38, F	Pain in left buttock	Posterior excision
McLanahan and Stone	1934	Presacral enterogenous cyst	Enteric cyst	48, F	Lump in rectum	Posterior excision
McLanahan and Stone	1934	Presacral enterogenous cyst	Enteric cyst	1 mo., M	Vomiting and constipation	Aspiration and subsequent posterior excision
Thomason	1934	Cyst of postanal gut	Cyst of intestinal origin	34, F	Pain, draining sinus	Repeated posterior excision
Raven	1935	Cyst of postanal gut	Cyst lined with stratified columnar and ciliated epithelium	2½ mo., F	Acute obstruction	Demonstrated at autopsy
Guis and Stout	1938	Cyst of vestigial gut	Cyst of intestinal origin	26, F	Pain and pressure in rectum	Intrarectal marsupialization
Guis and Stout	1938	Cyst of vestigial gut	Cyst of intestinal origin	36, F	None found on routine exam.	Posterior excision
Ladd and Gross	1940	Duplication of rectum	Cyst of intestinal origin with mixed mucosa	6 mo., F	Recurrent obstruction	Repeated aspiration and subsequent posterior excision
Custer, et al.	1946	Enterogenous cyst involving rectum	Enterogenous cyst	29, M	Symptoms of bladder pressure	Excision by laparotomy

REVIEW OF LITERATURE

We have been able to find ten cases of histologically proven presacral enterogenous cysts reported in the literature. (Table I).

Middledorpf,[1] in 1885, was the first to describe a presacral cyst of intestinal origin. The patient was a one-year-old female, and when the cyst was removed by Kraske, it was found microscopically to have all the structure of intestinal wall. Diagnosis: cyst of postanal gut origin.

In 1932, Ballantyne[2] reported a presacral cyst in a female of 38 years. The cyst contained 475 cc. of fluid and was removed by posterior excision. Microscopically, the cyst was lined with columnar epithelium. Goblet cells secreting mucin were present. There was a small area showing adenocarcinoma. Diagnosis: cyst of postanal gut with area of adenocarcinoma.

In 1934, McLanahan and Stone[3] described two cases of presacral enterogenous cyst. The first case was a woman of 48 years who complained of a lump in the rectum which at times would protrude from the anus but was easily reduced. Digital examination revealed a small cystic mass lying about two inches within the anal orifice and situated between the posterior wall of the

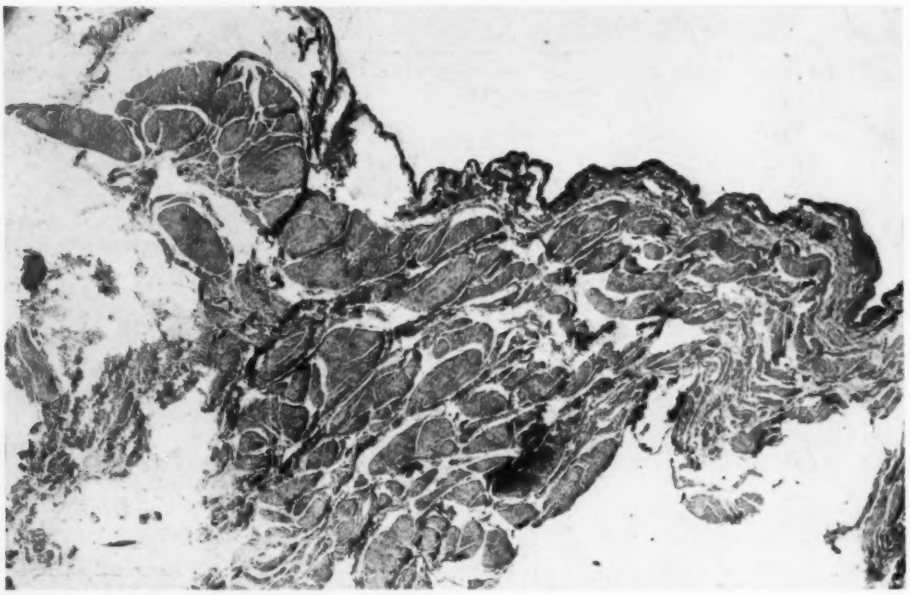

FIG. 2.—Low power microphotograph of cyst wall demonstrating the different layers of epithelium, subepithelium, and muscularis.

rectum and the coccyx. The mass was about the size of a walnut, was fluctuant, freely movable and not tender. Doctor Stone removed the tumor by posterior excision after the coccyx was resected. The mass was dissected from the posterior rectal wall, to which it was closely attached. Microscopic examination of the cyst wall showed tall columnar epithelium of mucus-secreting type. The submucosa was composed of longitudinal and circular muscular layers covered by a layer of serosa. Diagnosis: enteric cyst.

The second case reported by McLanahan and Stone was in a one-month-old male infant with intestinal obstruction from a mass filling the rectum. The mass was thought to be an intussusception, but on exploration of the abdominal cavity, a fluctuant mass the size of a golf ball was found below the peritoneal reflexion. The abdominal wound was closed, and on the following day the tumor was aspirated by needle entering the skin one inch to the right of the

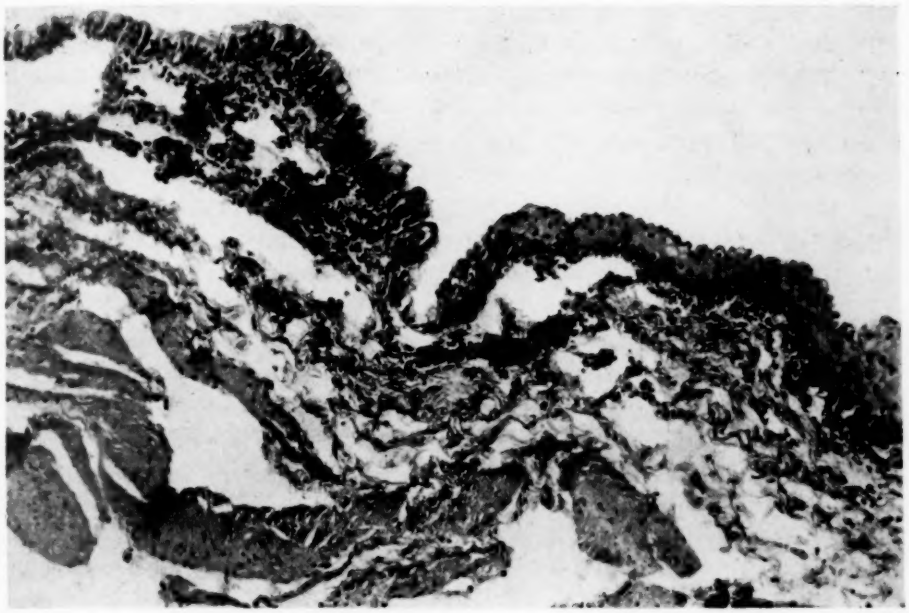

FIG. 3.—Metaplasia from columnar to squamous epithelium. Notice mucus droplets within the cytoplasm of columnar cells (proven by use of mucicarmin stain).

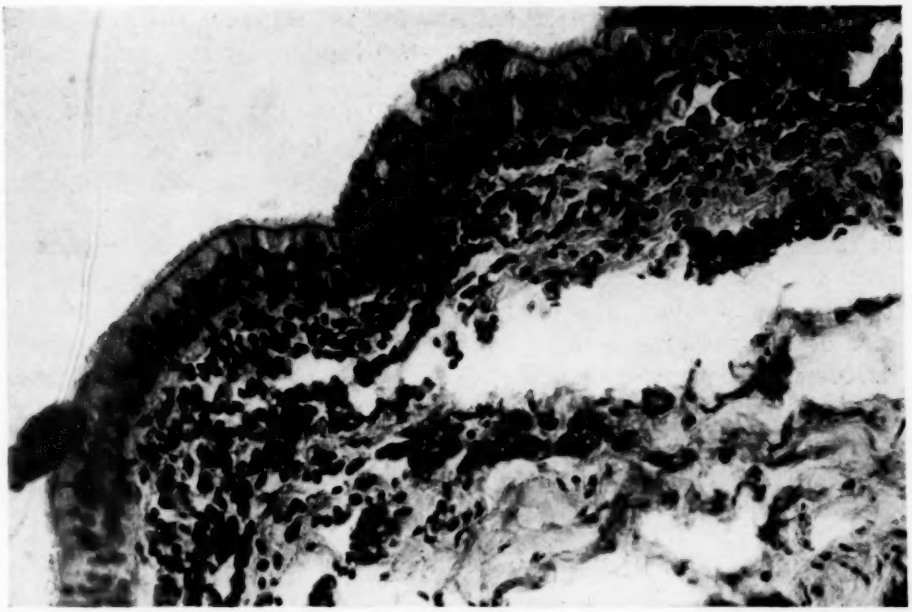

FIG. 4.—Cuticulum of columnar epithelium demonstrated by the use of iron-hematoxylin stain.

posterior margin of the anus. Twenty-five cc. of cloudy fluid were withdrawn, and the obstruction was temporarily relieved. The cyst was aspirated on five occasions in the next month, and the condition of the baby so improved that posterior excision of the cyst was performed. The microscopic sections showed a well-defined mucosa lined with columnar epithelium of mucus-secreting type. The outer wall was composed of two circular and longitudinal muscle layers covered by serosa. Diagnosis: enteric cyst.

Thomason,[4] in 1934, reported a case of sacro-coccygeal cyst of the postanal gut. His patient was a 34-year-old woman with a draining sinus near the tip of the coccyx which had been present since a mass in that area was incised and drained several years before. The sinus tract and the cyst were removed by posterior excision. Microscopic examination showed the wall of the cyst to be made up of columnar epithelium of the mucus-secreting type, Peyer's patches and two layers of smooth muscle. Diagnosis: postanal gut cyst.

Raven's[5] case, reported in 1935, was a 2½-month-old female who was acutely obstructed by a retro-rectal cyst. The condition was thought to be an intussusception, and laparotomy was performed. At autopsy the mass was removed and microscopic sections showed the cyst to be lined with several layers of epithelium, the innermost being ciliated columnar epithelium. Diagnosis: cyst of postanal gut.

Guis and Stout[6] reported two cases in 1938. The first was a 26-year-old female who complained of rectal pain and pressure. A palpable mass posterior to the rectum was thought to be an abscess. An intrarectal incision was made and the tumor wall marsupialized from within after removing a part of the wall. Pathologic examination showed stratified and columnar epithelium with mucin secretion and smooth muscle layers. Diagnosis: cyst of vestigial gut origin.

The second case of Guis and Stout[6] was a 36-year-old female with a cyst in the postero-lateral rectal wall found on routine rectal examination. Posterior excision of the cyst was done and the pathologic examination showed smooth muscle and a mucosa which was composed of stratified squamous and ciliated columnar epithelium tending to form glands. Mucin was present. Diagnosis: cyst of vestigial gut origin.

Ladd and Gross[7] reported one case in 1940. They prefer the term "duplication of a part of the alimentary canal," but also use the term enterogenous cyst. Their patient was a female, age 6 months, who had recurrent bowel obstruction due to a presacral mass. This tumor was removed by posterior excision. The sections of the cyst wall showed mucosa, submucosa and the muscle layers characteristic of intestine. The mucosa showed mixed types of glands, some of colon and some of gastric type. Diagnosis: duplication of rectum.

Custer, Kellner and Escue[8] report one case in 1946. Their patient was a 29-year-old man complaining of pressure in the pelvis, epigastric pain and a decrease in urinary bladder capacity. Rectal examination disclosed a cystic mass which filled the pelvis. This mass was removed through a low midline

incision. Its attachment was to the anterior rectal wall. Pathologic examination showed the cyst wall to be made up of tall columnar mucus-secreting epithelium and a well-defined layer of smooth muscle. Diagnosis enterogenous cyst.

ETIOLOGY

Three theories have been advanced to explain the presence of enterogenous cyst.

Middledorpf,[1] in reporting his case of enterogenous retro-rectal cyst in 1885, felt that the origin of the cyst was in the vestigial postanal gut. Five of the other authors reporting their cases chose to believe that this theory best explains the presence of the cyst in the midline between the coccyx and the rectum.

The diverticular theory of cyst origin is based on the work of Lewis and Thyng,[9] who demonstrated that diverticuli occur frequently in all portions of the digestive tube of the embryo. These may become occluded at the neck and the cyst results.

A third theory, known as the sequestration theory, suggests that a group of cells becomes pinched off from the primordial intestinal tube and undergoes subsequent development outside the lumen of the intestine.

PATHOLOGY

Although the term "enterogenous" or "enteric" cyst has become accepted when applied to these tumors, they are perhaps more accurately named "duplications of the alimentary tract" as suggested by Ladd and Gross.[7] Their term is actually the requirement for pathologic diagnosis of these cysts.

As Ewing[10] pointed out, the most variable component is usually the mucosal lining, which may show cylindrical, cuboidal, stratified or flat epithelium. The degree of tension within the cyst, together with the amount of inflammatory reaction, produce many variations in the type of mucosa. Ladd and Gross,[7] in reporting their case of presacral cyst, pointed out that the mucosa may be typical of that segment of the bowel to which it is adjacent or it may be typical of some bowel segment far removed from the cyst. The mucosa may be mixed, as in their case, showing large bowel and gastric mucosa.

The presence of intestinal mucosa, smooth muscle layers, nerve bundles and serosa establish the origin of the cyst to be enteric. The serosal layer is usually absent when the cyst is presacrally located.

TREATMENT

The treatment in reported cases has been aspiration, incision and drainage through the rectum, marsupialization and removal by intra-abdominal approach or posterior excision. All authors advise removal as a necessity in some cases and as a guard against malignant degeneration. The removal of the cyst usually can be accomplished by the removal of the coccyx in a posterior approach.

We wish to acknowledge our indebtedness to Dr. Phillip R. Rezek for the pathologic report in this case.

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DISCUSSION.—DR. G. V. BRINDLEY, Temple, Texas: I am sure all of you have enjoyed this excellent paper, for it is a most interesting presentation of one of the infrequent tumors which originate in and ventral to the sacrum. The caudal area is the location for many pathologic types of cysts, tumor, sinuses and fistulas which usually arise from vestigial embryonic tissue.

Some seven years ago, within a period of 14 months I encountered three neoplasms which originated ventral to the sacrum. It was my privilege to present these cases before this Association four years ago. One of these growths was a chordoma, another was an ependymal cell glioma, and the third was a large dermoid cyst. Since statistical data show that most patients with chordoma do not remain well, it was believed that it probably would be of interest to report at this time that the patient who had the chordoma is well and apparently free of disease. It is now eight years since the neoplasm was removed.

May I mention three facts worthy of emphasis pertaining to tumors of this region. The first is that diagnosis of most of these neoplasms depends upon a careful vaginal and/or rectal examination. Certainly no physical examination is complete unless these examinations are performed. Another fact deserving comment is that these tumors are cured only by complete removal. To attempt to cure a cyst of this region by incision and drainage usually results in secondary infection and a persisting sinus. Furthermore, adequate exposure is essential for removal of these lesions. The complete excision of a growth of this region is facilitated by the proper approach, which is obtained by an incision over the sacrum and coccyx extending to near the anus. The patient should usually be in the Kraske position. The coccyx and as much of the sacrum below the sacroiliac articulation as is necessary for adequate exposure of the neoplasm should be removed, together with the muscles and nerves of this region.

It should be appreciated that the segment of the sacrum below the sacroiliac articulation, together with the coccyx and all the sacral nerves except the first and second, can be removed without severe disability being incurred by the patient.

Again, let me congratulate the essayist upon this fine presentation.

DR. HARVEY STONE, Baltimore: I want to thank Doctor Perry for putting this case in the record, because it seems to me that, in view of his study of the literature to date, anyone encountering such a condition as this should record it, because of our scanty infor-

mation about these cysts. At the same time, I feel sure that his finding only 11 such tumors in the literature bears no real relationship to the frequency of occurrence, because there must be many cases unrecorded. While the total figures involved are too small to be of statistical significance, it is remarkable that of 11, nine were in females. Whether that means anything I am not prepared to say. Four patients presented themselves with symptoms of intestinal obstruction, of greater or less degree. This is highly significant; it means that the tumor must have slowly grown to a size that made it mechanically obstructive over a considerable period of time; ordinarily these tumors do not cause obstruction.

I want to repeat what was said about the surgical approach. I feel first that complete removal is the only satisfactory treatment. Second, that the proper approach is from below and behind, with a vertical incision posterior to the anus, with removal not of the coccyx alone but of a sufficient amount of the sacral body to get adequate exposure of the tumor. The amount to be removed is to be determined by the size of the mass. And, finally, it is important in doing the operation not to perforate into the rectum and not to damage the sphincter.

ANNOUNCEMENT

Beginning with the first issue of Volume 130 of the ANNALS OF SURGERY, July, 1949, the Editorial Board plans to publish signed editorials in each monthly issue. The editorials will be written (to begin with) by members of the Editorial or Advisory Boards. These editorials are not intended to be summaries of recent advances in surgery, nor are they intended to be short original articles on scientific subjects. They will, rather, express the opinions of the authors on matters of general interest to the surgical profession which do not ordinarily appear in scientific articles.

JOHN H. GIBBON, JR., M.D.,
Chairman, Editorial Board.

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The conditions annexed by the testator are that the prize "shall be awarded every five years to the writer of the best original essay, not exceeding one hundred and fifty printed pages, octavo, in length, illustrative of some subject in Surgical Pathology or Surgical Practice founded upon original investigations, candidates for the prize to be American citizens."

It is expressly stipulated that the competitor who receives the prize shall publish his essay in book form, and that he shall deposit one copy of the work in the Samuel D. Gross Library of the Philadelphia Academy of Surgery, and that on the title page it shall be stated that to the essay was awarded the Samuel D. Gross Prize of the Philadelphia Academy of Surgery.

The essays, which must be written by a single author in the English language, should be sent to the "Trustees of the Samuel D. Gross Prize of the Philadelphia Academy of Surgery, care of the College of Physicians, 19 South 22nd Street," on or before January 1, 1950.

Each essay must be typewritten, distinguished by a motto, and accompanied by a sealed envelope bearing the same motto, containing the name and address of the writer. No envelope will be opened except that which accompanies the successful essay.

The Committee will return the unsuccessful essays if reclaimed by their respective writers, or their agents, within one year.

The Committee reserves the right to make no award if the essays submitted are not considered worthy of the prize.

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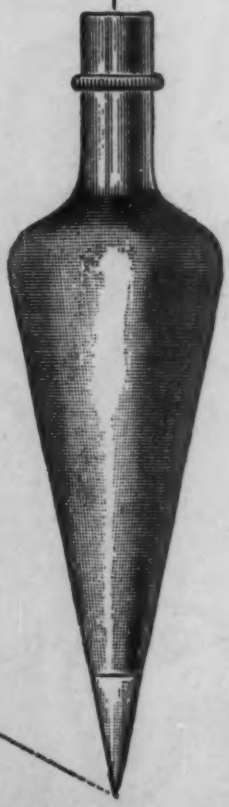

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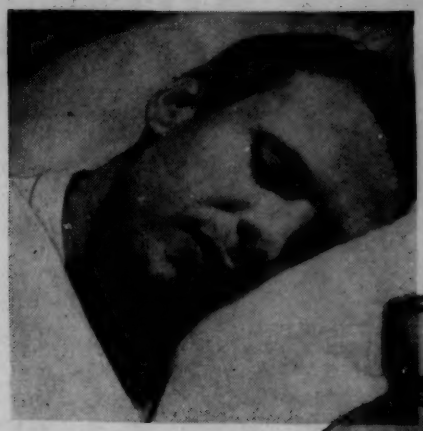

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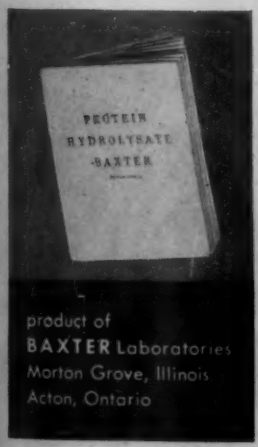

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Patients should be closely observed until optimal dosage is established, for possible paradoxical effects or orthostatic hypotension.

1. Grimson, Marzoni, Reardon and Hendrix: Ann. of Surg., 127: 5, May, 1948.
2. Reich, N. E.: Med. Times, Jan., 1949.

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